



# American Pharmacists Association<sup>®</sup>

Improving medication use. Advancing patient care.

February 13, 2015

The Honorable Fred Upton  
2183 Rayburn House Office Building  
Washington, DC 20515

**RE: 21<sup>st</sup> Century Cures Discussion Draft**

Dear Chairman Upton:

APhA, founded in 1852 as the American Pharmaceutical Association, represents more than 62,000 pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care. APhA members provide care in all practice settings, including community pharmacies, hospitals, long-term care facilities, community health centers, managed care organizations, hospice settings and the uniformed services.

We thank the Committee for the opportunity to provide input on the 21<sup>st</sup> Century Cures discussion draft. APhA fully supports the Committee's goals of advancing medical research and accelerating innovation to support the development of new treatments and technologies. Further, we were pleased to see an emphasis on support for young clinicians, data transparency, improved communication, as well as a focus on improved public health through enhanced vaccination programs in the draft legislation. While APhA supports the draft legislation as a whole, we have concerns regarding the impact of Sections 4281 and 4282 on patient safety and access, as well as some recommended changes to the language in Sections 2092, 2301, and 4141, as detailed below.

**A. Sections 4281 and 4282 May Result in Decreased Patient Access to Pharmacy Services**

*Sec. 4281: Establishing PDP Safety Program to Prevent Fraud and Abuse in Medicare Prescription Drug Plans.* APhA believes that the prevention of fraud, waste, and abuse is of paramount importance, but has serious concerns about the impact of the proposed provision on patient access to medically-necessary medications. As drafted, the provision states that a patient's access to "some or all classes of covered Part D drugs" may be restricted to a specific "safe pharmacy network." While we appreciate the inclusion of a list of factors to be considered when structuring networks, restricting all of the patient's medications seems unnecessary, particularly as the provision is keyed to "frequently abused" medications. Additionally, the provision allows prescription drug plans (PDPs) and/or the Secretary to determine the criteria for "safe pharmacy networks" without input from other clinicians. Pharmacists are active partners in the fight against substance abuse and, along with other clinicians, must be fully engaged in discussions regarding the creation and maintenance of such networks to ensure that legitimate medication users are not harmed. Finally, while APhA understands the need to prevent individuals who are not using medication legitimately from "plan-hopping", we question the efficiency of reporting information regarding individuals enrolled in "safe pharmacy networks" to

the Secretary and then, as provided by section (B), tasking the Secretary with reporting that information to the plans. We are concerned that the extra channels this approach creates (versus a plan-to-plan communication structure) could compromise patient privacy.

*Section 4282: Part D Suspension of Claims Payment.* As stated above, APhA supports efforts to combat fraud, waste, and abuse, provided that such efforts are balanced with patient access requirements. APhA strongly opposes this provision because it offers PDPs broad discretion to suspend payment to pharmacies indefinitely on the basis of mere allegation, which could seriously compromise a pharmacy's operations, and by extension, possibly limit patient access to medically-necessary medications and services. The provision provides no defined right of appeal for a pharmacy, except stating in section (H)(i) that the Secretary has discretion "to determine there is not good cause for suspension of payment." Ceasing payment on the basis of unsubstantiated allegations without a defined method for immediate appeal raises due process concerns. Further, the definition of "credible allegation" provided in (H)(ii) is far too broad and sets the bar too low for such a serious punitive action. The provision provides three "credible" sources of evidence, including "a complaint made on a Medicare fraud hotline" and "detection of potential fraud through the analysis of claims data." Anonymous complaints can be made for myriad reasons, and while they should be investigated, payment should not be suspended on the basis of mere hearsay. Additionally, we also have concerns about how "analysis of claims data" will be accomplished. APhA opposes the use of sampling and extrapolation due to high error rates—any analysis not based on the review of actual claims could be seriously flawed. Finally, the provision offers no time limitations on claims suspension or any recourse to pharmacies that may suffer serious financial damage as a result of inappropriate, erroneous, or bad faith claims suspension. Based on the foregoing, APhA requests that the Committee remove Section 4282 in its entirety. APhA would be happy to assist in the Committee in identifying solutions that protect against Medicare fraud and abuse without jeopardizing pharmacy operations and, consequently, patient access.

## **B. Recommended Changes for Sections 2092, 2301, and 4141**

*Section 2092. Recommendations for Development and Use of Clinical Data Registries.* APhA commends the Committee for requiring that the Secretary make recommendations for the development and use of clinical data registries. In developing standards for registries, we strongly encourage the Secretary to consult with all of the clinicians on the health care team, including pharmacists, who have historically been excluded from participation in these discussions. A repository of stored and shared clinical data will aid in the meaningful exchange of information between and among clinicians reporting to these registries. Pharmacists report clinical data, including immunization records and controlled substance fills, to registries, where it can be viewed by a wide array of health care providers. Despite their vital role on the health care team, pharmacists currently lack access to clinical data that other health care providers report to registries. Access to comprehensive information is essential because it would allow pharmacists to make the most informed clinical decisions possible, which, when considering allergies and drug-drug interactions, may mean the difference between life and death. We ask that the Committee require the Secretary to outline standards for the bidirectional, interoperable exchange of information between the electronic health records of the reporting clinicians and registries and require registry access for pharmacists.

*Sec. 2301: Precision Medicine.* APhA believes that pharmacists play a key role in the delivery of precision medicine. While significant advances in precision medicine have been made for select cancers, the practice is not currently in use for most diseases. Pharmacists are prepared and ready to help expand the practice of precision medicine to many other health conditions, taking

into account the individual's genetic, environmental, and lifestyle variables. With access to patients' genetic information and reimbursement for review of the data, pharmacists could offer patients a more comprehensive, tailored and enhanced medication therapy management service.

*Section 4141: Coverage of Certain Disposable Medical Technologies Under the Medicare Program.* In general, APhA supports patient access to novel medical technologies, provided they are medically effective. However, it is unclear what would qualify as "disposable medical technology" under section 4141, as broad discretion is left to the Secretary to make those determinations. Because we can only speculate as to which technologies might fall under this section, it is difficult to determine if the specified payment methodology would be sufficient to make provision of these items financially feasible for pharmacies. Given that these changes could have repercussions for patients and pharmacies, we ask that the Committee revise this provision to direct the Secretary to solicit stakeholder feedback before implementing the changes, ideally through notice-and-comment rulemaking. This will allow patients, clinicians, and other interested parties to provide more targeted, substantive feedback prior to implementation.

Thank you for the opportunity to provide comments on the 21<sup>st</sup> Century Cures discussion draft. As you move forward, please do not hesitate to use APhA as resource. If you have any questions or require additional information, please contact Michael Spira, Senior Lobbyist, Government Affairs at [mspira@aphanet.org](mailto:mspira@aphanet.org) or by phone at (202) 429-7507.

Sincerely,



Thomas E. Menighan, BSPHarm, MBA, ScD (Hon), FAPhA  
Executive Vice President and CEO

cc: Stacie Maass, BSPHarm, JD, Senior Vice President, Pharmacy Practice and Government Affairs  
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#### Combined Sections Meeting

February 4-7, 2015  
Indianapolis, IN

February 10, 2015

The Honorable Fred Upton  
Chairman,  
Committee on Energy and  
Commerce  
2125 Rayburn Office Building  
Washington, DC 20515

The Honorable Diana Degette  
Committee on Energy and  
Commerce  
2368 Rayburn Office  
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Washington, DC 20515

Dear Chairman Upton, Representative Degette, and Members of the Energy and Commerce Committee:

On behalf of more than 90,000 physical therapists, physical therapist assistants, and students of physical therapy, the American Physical Therapy Association (APTA) thanks you and members of the Energy and Commerce Committee for the opportunity to participate in the dialogue regarding the 21<sup>st</sup> Century Cures discussion draft. APTA commends your leadership and extensive work on this initiative and is happy to provide the below recommendation's regarding the discussion draft:

### **Telehealth**

Physical therapists provide critical services to beneficiaries under Medicare to assist individuals remain in their homes, communities and society at their highest potential functional level. In many ways, telehealth is still an untapped resource in redefining how health care is delivered and although great advancements have been made in this sector, much work remains to realize the full potential of this delivery mechanism.

### **Definition of Telehealth Providers**

APTA encourages the Committee to amend language in the discussion draft to specifically indicate which providers can be considered by the Secretary for telehealth coverage. Due to the vague nature of section 1834 (m)(4)(F), there may be unintended consequences if the statute is not amended to clearly define providers that may receive reimbursement for services delivered via telehealth. APTA calls to the working group's attention two specific solutions to rectify this issue.

- 1) Utilize the same definition of service providers as outlined under the Physician Quality Reporting System:

Section 1848(k)(3)(B):

(B) Eligible professional.—The term “eligible professional” means any of the following:

(i) A physician.

(ii) A practitioner described in section 1842(b)(18)(C).

(iii) A physical or occupational therapist or a qualified speech-language pathologist.

(iv) Beginning with 2009, a qualified audiologist (as defined in section 1861(l)(3)(B))

- 2) Specifically cite which services the working group would like to add to section 1834. The *Medicare Telehealth Parity Act of 2014* (H.R. 5380- 113<sup>th</sup> Congress) provides an example of how this could be accomplished:

Additional covered telehealth services.—Section 1834(m)(4)(F)(i) of the Social Security Act (42 U.S.C. 139m(m)(4)(F)(i)) is amended by adding at the end the following new sentence: “Beginning on [date], such term shall include respiratory services, audiology services (as defined in section 1861(l)), and outpatient therapy services, including physical therapy, occupational therapy, and speech-language pathology services.”

### **Coverage of Services**

As you know, Medicare provides for limited coverage of telehealth services and physical therapists are not currently eligible providers under Medicare for reimbursement of these services. Though APTA understands the committee’s intent to avoid increased expenditures in the Medicare system, we would ask for your consideration of language that either adds physical therapists as an eligible provider under Medicare or instructs the Secretary of Health and Human Services to specifically consider expanding eligible provider coverage to physical therapists in its consideration of new telehealth services as outlined in the discussion draft.

Many stakeholder groups have endorsed the idea of telehealth therapy coverage as the next thoughtful step in providing access to critical health care services. Further, APTA and other organizations, including the American Speech-Language-Hearing Association (ASHA) and the American Occupational Therapy Association (AOTA) have advocated to cover therapy services delivered via telehealth as a reimbursable service under Medicare. Legislation introduced in the 113<sup>th</sup> Congress, The *Medicare Telehealth Parity Act of 2014* (H.R. 5380), would require Medicare to reimburse physical therapists, speech-language pathologists, occupational therapists, audiologists, and respiratory therapists for services furnished to Medicare

beneficiaries. This legislation is broadly supported by many stakeholders in the health care community.

APTA is encouraged that the discussion draft also instructs the Secretary to consider episodes of care for potential coverage under Medicare. Beneficiaries who would benefit from care delivered via telehealth are more likely to avoid readmissions or expensive hospital stays if their care can be delivered with lower costs by more than one provider. It is currently nonsensical to only reimburse specific providers for utilizing telehealth. For example, if a patient is unable to travel or lives a great distance from medical facilities, it does not make sense to cover some services delivered via telehealth while denying coverage for others. Ultimately, this scenario does little for patient convenience or for the fiscal health of Medicare. APTA believes episodes of care delivered via telehealth have the potential to reduce Medicare expenditures but only if the full episode of care, including full coverage of all services in the episode, is deemed reimbursable.

### **Licensure Compacts and State Licensure Boards**

APTA is pleased to see language in the discussion draft that describes the sense of Congress that states should collaborate on the use of interstate or multi-state licensure compacts. However, we recommend that the working group amend this language to clarify that this work is not only done through state medical boards but through various state licensure entities. APTA, for example, is currently working with the Federation of State Boards of Physical Therapy to create a process by which state physical therapy licensure boards may engage in interstate licensure compacts. This work is well underway and is scheduled to be completed in 2015. We recommended removing the term “**medical**” in this section as this language could be misconstrued to only apply to physician licensure compacts. Instead we recommend the use of “**state licensure entities**” to more clearly express the sense of Congress that licensure compacts should be considered by both physician and non-physician licensure entities.

### **Rehabilitation Research**

Although not addressed in this discussion draft, we believe there is an opportunity to include provisions to advance rehabilitation research at the National Institutes of Health (NIH) within the 21<sup>st</sup> Century Cures Act.

NIH supports rehabilitation research through the National Center for Medical Rehabilitation Research (“NCMRR”) within the Eunice Kennedy Shriver National Institute for Child Health and Human Development (“NICHD”). In 2012, Dr. Collins, NIH Director, and Dr. Alan Guttmacher, NICHD Director,

established a Blue Ribbon Panel on Medical Rehabilitation Research at the NIH (“BRP”). The panel produced a report and recommendations to promote rehabilitation research in the future through the NIH Rehabilitation Research Plan which has been the subject of legislative efforts last Congress.

Rehabilitation and disability research is cross-cutting, multi-disciplinary, and focuses on restoring and improving functional capacity in individuals who have experienced an illness, injury, disability or chronic condition. This type of research also focuses on maintaining and preventing deterioration of functional skills and abilities in order to enhance quality of life and independent living.

Please find below APTA’s recommendations to add to the discussion draft as it relates to enhancing the stature of rehabilitation research at the NIH.

#### **Update the Trans-NIH Rehabilitation Research Plan**

APTA recommends that the Research Plan must include objectives, benchmarks, and guiding principles regarding the conduct, support, and coordination of medical rehabilitation research at NIH, consistent with the purpose of the Center. The Research Plan should be updated periodically or not less than every five years.

#### **Clarify the Respective Roles of the NCMRR Director, the Director of the Institute and the Director of NIH Regarding the Research Plan**

APTA advises to place the key subject matter expert (i.e., the NCMRR Director) at the helm of the Research Plan for conducting medical rehabilitation research at NIH while making it clear that the Director of the Center is exercising this authority on behalf of the Director of NIH and the Director of the Institute and in consultation with the Medical Rehabilitation Coordinating Committee (coordinating committee) and the National Advisory Board on Medical Rehabilitation (advisory board) established by statute.

#### **Add an Annual Rehabilitation Research Progress Report**

APTA recommends that the Director of NCMRR, in consultation with the Director of the Institute, must prepare an annual report for the coordinating committee and the advisory board describing and evaluating the progress made during the preceding fiscal year in achieving objectives, benchmarks, and guiding principles included in the Research Plan. In preparing the report, the Director of the Center and the Director of the Institute must consult with

the Director of NIH and the report must reflect an assessment of the Research Plan by the Director of NIH.

### **Add a Scientific Conference or Workshop on Medical Rehabilitation Research**

APTA recommends that the coordinating committee periodically, or not less than every 5 years, host a “scientific conference or workshop on medical rehabilitation research” in connection with updating of the Trans-NIH Medical Rehabilitation Research Plan. This policy ensures periodic review of the state of medical rehabilitation science and outreach to the research community in connection with revisions of the Research Plan.

### **Improving Stature of Medical Rehabilitation Science**

APTA recommends that the coordinating committee includes the Director of the Division of Program Coordination, Planning, and Strategic Initiatives in the Office of the Director of NIH and the coordinating committee is chaired by the Director of the Center, acting in the capacity of a designee of the Director of NIH. This policy is intended to maximize the likelihood that the trans-NIH nature of medical rehabilitation research is realized.

### **Clarify Funding Among NIH Agencies**

APTA recommends that the Director of the Center, in consultation with the Director of the Institute, the coordinating committee, and the advisory board, must develop guidelines governing the funding of medical rehabilitation research by the Center and other agencies of the NIH. These guidelines should ensure that funding initiatives reflect the purposes of the Center and are consistent with the Research Plan. This policy is intended to establish funding grant procedures that focus on a common understanding of medical rehabilitation research needs.

### **Include a Definition of Medical Rehabilitation Research**

Because current law does not include a definition of the term “medical rehabilitation research,” we recommend including a definition as: “The science of mechanisms and interventions that prevent, improve, restore, or replace lost, underdeveloped, or deteriorating function (defined at the level of impairment, activity, and participation according to the World Health Organization in the International Classification of Function, Disability, and Health (2001).” This definition is consistent with the Blue Ribbon Panel recommendations and would facilitate a consistent understanding of medical rehabilitation science at NIH.



**Improvements in the Medicare Local Coverage Determination Process**

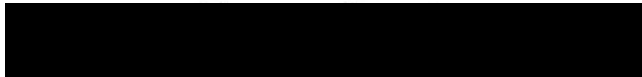
APTA is pleased to see the inclusion of provisions to improve the local coverage determination (LCD) process in the future. We would also recommend the Committee consider that other providers, including a physical therapist, be represented on the Carrier Advisory Committee (CAC) to have representation from those effected by the proposed limitation in coverage. Currently these meetings include only physicians, which remains a concern as they are not representative of those providing the services. APTA would appreciate if this was addressed by the Committee in this legislative text.

**Conclusion**

Again, thank you for your attention to this issue. APTA stands ready to assist the Committee and would be pleased to provide additional information on the topics listed above. If the working group has any questions or need additional resources, please contact Monica Massaro, Senior Congressional Affairs Specialist at [monicamassaro@apta.org](mailto:monicamassaro@apta.org) or 703-706-3156.

Thank you for the opportunity to provide recommendations.

Sincerely,

A black rectangular redaction box covering the signature of Paul A. Rockar, Jr.

Paul A. Rockar, Jr, PT, DPT, MS  
President

PAR: mkm



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February 9, 2015

The Honorable Fred Upton  
Chairman  
Committee on Energy and Commerce  
U.S. House of Representatives  
Washington, DC 20515

The Honorable Frank Pallone, Jr.  
Ranking Member  
Committee on Energy and Commerce  
U.S. House of Representatives  
Washington, DC 20515

Dear Chairman Upton and Ranking Member Pallone:

On behalf of the members of the American Podiatric Medical Association (APMA), the national organization representing the vast majority of America's podiatric physicians and surgeons, I am writing today in support of the Ellmers-Butterfield provision in the 21st Century Cures Discussion Draft bill, "Subtitle G—Disposable Medical Technologies."

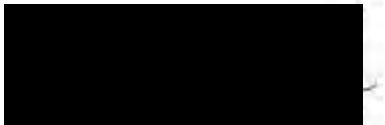
As physicians and surgeons of the lower extremities, podiatrists are dedicated to incorporating the highest quality of treatments and technologies in delivering medical care to patients. But unfortunately, current Medicare law is antiquated by not covering certain disposable technologies in the home care setting that may be more cost-effective, promote greater patient compliance, and lead to improved outcomes.

These disposable technology items are commonly reimbursed by private payers, as they are easier to use, less expensive, and provide comparable outcomes. Many of these technologies are smaller and designed for single-patient use. They may last a few days, weeks, or months, but not years.

The outdated Medicare definition of DME precludes consideration of these modern technologies suited for home-based care. By providing coverage for disposable medical technologies in the home, Medicare would promote continuity of care between care settings, facilitate better outcomes, reduce costs, and enhance system efficiencies. Moreover, Medicare coverage would ensure that patients do not lose access to these technologies as they transition from private insurance at age 64 to Medicare at age 65.

As Congress considers policy options to modernize Medicare, the Disposable Medical Technologies provision deserves to be part of the discussion. APMA looks forward to working with you and your colleagues to advance this important initiative.

Sincerely,



President

Hi Katie,

I hope this finds you well. After reviewing the 21st Century Cures discussion draft, we'd like to provide the following comments and recommendations. We deeply appreciate your review, and please don't hesitate to ask us any questions. We are also thankful for openness of this process and the great effort Chairman Upton has put into outreach and communication in the last year. You all must be extraordinarily busy! With that said, I'd address the following areas:

Section 4008, Additional Funding for NIMH BRAIN Research

The BRAIN Initiative promises significant breakthroughs to treat neurological diseases, including mental illness and substance use disorders, which require technological innovations to develop new ways of mapping neurological pathways. APA is appreciative of Chairman Upton for the inclusion of this provision, and for O&I Subcommittee Chairman Murphy for spotlighting the issue in his years long mental health investigation - as the committee's document references. However, Dr. Murphy's Helping Families in Mental Health Crisis Act (H.R. 3717) calls for this authorization boost to include both the BRAIN Initiative and "research on the determinants of self and other directed violence in mental illness, including studies directed at reducing the risk of self harm, suicide, and interpersonal violence". These research activities are a critical piece of an overall strategy to better address care for individuals in mental health crisis. **APA recommends that the proposed authorized funding increase to NIMH include support for violence prevention research as suggested by H.R. 3717.**

Subtitle I: Telemedicine

APA absolutely supports efforts to increase access to telemedicine for Medicare beneficiaries and other underserved population. This technology holds particular promise for the delivery of mental health care. We are appreciative of the discussion draft's removal of the geographic restrictions that arbitrarily limit access to appropriate telemedicine services. However, we echo concern from the medical community that **the broad waiver language in Subtitle I should be modified to expressly prevent waiver of state-based licensure requirements and other scope of practice related billing requirements currently required by the Medicare program.**

Subtitle K: Cures Acceleration Network (NCATS enhancement)

The National Center for Advancing Translational Sciences (NCATS) is the newest of 27 Institutes and Centers at NIH, and it was established in December 2011 to catalyze innovative methods and technologies to enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human illnesses. We are excited about the potential NCATS holds for aiding the development of treatments for mental illness and substance use disorders. **APA supports the proposed NCATS authorized funding increase in the discussion draft and encourages its inclusion in future iterations of Cures.**

Subtitle S: Continuing Medical Education Sunshine Exemption

The importance of up-to-date, peer reviewed scientific medical information as the foundation for good medical care is well documented. Scientific peer-reviewed journal reprints, supplements, and medical text books have long been considered essential tools for clinicians to remain informed about the latest in medical practice and patient care. There is widespread consensus that CMS' recent proposal on Sunshine Act implementation will harm the dissemination of clinically relevant and critical medical knowledge that improves and enhances patient care. **APA strongly supports this provision and encourages its inclusion in future iterations of Cures.**

In general, The shrinking pipeline for innovative psychiatric medications

It is clear that psychiatry is facing a prolonged drought in the development of groundbreaking medications. One by one, major pharmaceutical companies have slashed or abandoned neuropsychiatric research programs. Meanwhile, there are huge unmet clinical needs in mental disorders including substance use disorder. According to industry leaders assembled for the American Psychiatric Foundation's recent "Pipeline Summit", psychiatric research and development programs have gained a high-cost, high-risk, and no-return reputation in industry after dozens of failed programs. While pharmaceutical interventions have been markedly improved to reduce unwanted side effects that inhibit treatment adherence, there have been few breakthroughs since the development of modern antidepressant and antipsychotic class medications in the 1980s and 1990s. This sober assessment must be contrasted with the striking toll that mental illness takes on patients, their families, and government budgets. As you know, mental illness is the leading cause of disability in the United States, with half of all chronic mental illness beginning by age 15, and three-quarters by age 25. The presence of a psychiatric disorder in medical and surgical patients increases the likelihood of hospital readmission, and psychiatric disorders account for 3 of the top 10 diagnostic categories of Medicaid "super-utilizers". That is why APA supports incentives including market exclusivity options, patent extension, and data package protections that encourage development of the next generation of groundbreaking psychiatric treatments. We hope to continue the dialogue on these issues with the Committee as the 21<sup>st</sup> Century Cures process moves forward.

Please let me know if you have any questions or if you'd like to discuss these matters further. Have a great weekend.

Best,  
Matt

**Matthew Sturm**

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**Comments by the American Society for Biochemistry and Molecular Biology to the  
Energy and Commerce Committee  
Request for Comments on “21<sup>st</sup> Century Cures Act” Discussion Draft  
February 10, 2015**

We applaud the work of the U.S. House Energy and Commerce committee on the 21<sup>st</sup> Century Cures initiative. The ASBMB has been involved in the conversation surrounding this initiative as we commented on two previous white papers from the committee, and we appreciate the opportunity to comment on this discussion draft. We look forward to being a part of this process as it moves forward.

Our members are basic researchers funded primarily by the National Institutes of Health. Thus, we have restricted our comments to the sections that would most affect our members. Sections not discussed here should not be construed as support of those sections.

**Sec. 2001 – Innovative Cures Consortium**

Our concern: This section would establish a nonprofit organization that issues grants to organizations for speeding the development and delivery of lab discoveries. However, the granting activity of this NPO is set up to run almost exactly like the largely successful STTR program. The proposed NPO and the STTR program grant money to small companies and nonprofit organizations. And both require the organization receiving the grant to commit its own resources to the funded project. Furthermore, those eligible for funding from this new NPO would be the same population as those eligible for NIH STTR support.

Our recommendation: To avoid a duplication of efforts and increasing bureaucracy, we suggest replacing the language creating this new NPO and rewriting the section to authorize money specifically for the NIH STTR program. Alternatively, should the NPO remain in the legislation, we encourage the committee to include language that would clearly delineate the roles of this NPO relative to STTR programs.

**Sec. 2241 – Plan for longitudinal study on outcomes of patients with a chronic disease**

Our concern: This section directs the NIH to identify a chronic illness, report on the state of research on that disease and design and execute a longitudinal study of that disease with the goal of generating new treatments and cures for that disease. However, dictating that the NIH or other agencies pick one of subset of diseases to build a research repertoire around damages research into other diseases. Furthermore, the dedicated research program has no guarantee of success. Research works best when scientists are competing for grants that are awarded based on exemplary, peer-reviewed grant applications. Congressionally directed research into a disease, even with as vague of a directive stated here, is a gamble of taxpayer dollars that are better spent supporting investigator-initiated research.

Our recommendation: Rewrite this section to have the NIH report on all long-term studies of chronic diseases omitting any plan for a long-term research project. Congress should then work with the scientific community and the NIH to find ways to incentivize research into understudied diseases.

**Sec. 2261 – Funding research by emerging scientists through Common Fund**

Our concern: This section would stop the transfer of money from NIH to AHRQ through what is commonly called “the tap.” The money saved by the NIH would be directed to funding “emerging scientists.” We have several concerns with this section.

- (1) The diversion of money from AHRQ damages the research community as a whole. All research is interconnected. AHRQ ensures that the discoveries made by NIH-funded researchers that turn into FDA-approved products are delivered and being used in the most effective and efficient ways possible. This type of research is critical for the NIH, CDC and FDA to improve on these products and ensure that they are available to all who need them. Furthermore, the goal of the 21<sup>st</sup> Century Cures initiative is to improve not only the path from discovery through development and delivery, but also to improve how patient feedback affects research and discovery.<sup>1</sup> The work of AHRQ is critical for this second part. It is not clear how the 21<sup>st</sup> Century Cures initiative benefits from potentially reducing the effectiveness of AHRQ.
- (2) On p.219, line 1, the definition of an “emerging scientist” differs substantially from the NIH’s definition of an Early Stage Investigator. Introducing a new class of investigator on top of a very similar class will cause confusion in the community and lead to inefficiencies in grant awarding and data analysis.
- (3) It is not clear why money is being diverted to “emerging scientists” in the manner indicated here. (1) The NIH policy of ensuring Early Stage Investigators have a fair shot at receiving grant money has been largely successful—grant applications from ESIs have nearly the same chance of success as established investigators.<sup>2</sup> (2) It is generally assumed that Early Stage Investigators have a difficult time securing their second NIH grant. If helping scientists secure their second grant is the point of this section, the legislation should be rewritten to clearly address this.

Our recommendation: The following section, Sec. 2262, requires the NIH to report on aging trends in the biomedical workforce. This report should be completed before any legislative attempts are made at funding specific constituencies within the workforce. Doing so may only introduce more problems. Furthermore, we feel the goals and funding mechanism of this section are misguided. As such, we recommend Sec. 2261 be removed from the final legislation. If this section remains, then we recommend:

- (1) If the goal of turning off the tap is to give the NIH more money, we recommend instead authorizing and appropriating more money for the NIH.
- (2) The legislation should conform to preexisting definitions of Early-Stage Investigators at the NIH and drop the “emerging scientist” nomenclature. On the other hand, if the point of (b)(2) is to make it easier for young scientists to win their second major award from the NIH, then the legislation should be clarified and written specifically toward that population of scientists. Furthermore, data on these scientists should be included in the report specified in Sec. 2262.

#### **Sec. 2262 – Report on trends in age of recipients of NIH-funded major research grants**

We support the analysis of aging trends in NIH-funded researchers

Our recommendation: We have two recommendations: (1) We suggest language be included directing the NIH to also report on the Early Stage Investigator program and how scientists typically fare transitioning out of this program. (2) We suggest that the reports in this section be made prior to legislating significant changes to the biomedical workforce as in Sec. 2261.

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<sup>1</sup> <http://energycommerce.house.gov/cures>

<sup>2</sup> <http://report.nih.gov/nihdatabook/index.aspx>. “R01-Equivalent grants, New (Type 1): Success rates, by career stage of investigator”

#### **Sec. 2281 – High-risk, high-reward research program**

Our concern: This section directs all NIH institutes and centers to reserve money for high-risk, high-reward research. Forcing institutes and centers to fund this type of research, which is already done well by the Common Fund, will divert funding from other well established programs that fund many researchers doing excellent work. Furthermore, high-risk, high-reward research is often transdisciplinary. One of the reasons the Common Fund was created was to fund high-risk, high-reward, transdisciplinary research.

Our recommendation: To expand high-risk, high-reward research at the NIH, the legislation should be rewritten to authorize an increase to this type of research through the Common Fund. This should be a redistribution of funds within the Common Fund, as we do not support Sec. 4007, which would authorize more money for the Common Fund. In an otherwise stagnant budget environment, increasing overall funding for the Common Fund would negatively affect researchers funded by other NIH mechanisms.

#### **Sec. 4001 – NIH research strategic investment plan**

Our concern: This section directs the NIH to develop a strategic investment plan. We support the idea that the NIH should have a long-term plan for how its appropriations will be invested. However, we are concerned about the 10 Mission Priority Focus Areas described on p.243, line 7. The scientific research enterprise works at its best when undirected, investigator-initiated research is fully funded. We understand the urge to direct funds into a specific disease or area of research. However, funding initiatives in this manner is not a guarantee of success or even progress. Rather, the American biomedical research program should continue to be funded as it has in the past—by valuing the contributions of investigator-initiated research and relying on projects proposed by scientific experts.

Our recommendation: The language regarding the Mission Priority Focus Areas should be removed.

#### **Sec. 4002 – Biomedical research working group to reduce administrative burden on researchers**

We support work to relieve the administrative burden on researchers.

Our recommendation: In the 113<sup>th</sup> Congress, H.R.5056, which would have established an inter-agency working group to address administrative burden at all federal science funding agencies, passed the U.S. House. We recommend placing a provision in the 21<sup>st</sup> Century Cures Act that, should legislation similar to H.R.5056 create a government-wide working group on administrative burden at science funding agencies, the NIH-specific administrative burden working group specified in this bill be disbanded, and their work handed over to the government-wide working group.

#### **Sec. 4003 – NIH travel**

Our concern: Attending research conferences is an essential part of being a part of the scientific community. These events are not boondoggles, but rather these conferences provide forums for improving training, sharing results and ideas, and forming collaborations.

Our recommendation: NIH scientists should be able to travel to scientific conferences without restriction in order to appropriately contribute to the American scientific enterprise.

#### **Sec. 4004 – Increasing accountability at the National Institutes of Health**



Our concern: This section seeks to improve accountability at the NIH. However, the provisions in this section would not achieve this and would only add to bureaucratic processes that slow discovery research. Specifically,

- (1) Sec. 4004(b), p.251, line 7 would require institute and center directors to personally review and approve all awards. NIH-funded grants undergo rigorous peer review by eminent scientists in the field as well as evaluation by the institute's council. Adding another layer of review by the institute director is unnecessary given these two prior rounds of rigorous review. Furthermore, the time and effort required by a director to fulfill this directive would cripple his/her ability to direct the activities of the institute and significantly slow the groundbreaking research sought by the 21<sup>st</sup> Century Cures initiative.
- (2) Sec. 4004(b), p.251, line 10 requires that NIH-funded grants have goals that are of "a national priority and have public support." Biomedical research and its fruits are a national priority and this research enjoys widespread public support.<sup>3</sup> Asking this metric to be true on a grant-by-grant basis would require polling the public on which specific grant applications should be funded. This is not possible given the budget of the NIH, the time the director would have to spend ascertaining this information, and the scientific capabilities of the general public.
- (3) Sec. 4004(b), p.251, line 13 would ask institute directors to ensure that other agencies are not funding work that accomplish the same goal. Scientific results must be verifiable and reproducible in labs other than the one making the initial discovery. Scientists conducting research all trying to achieve the same goal is how we make sure that the scientific answers that are found are correct. Preventing multiple researchers from pursuing the same scientific goals is antithetical to research and the spirit of what the 21<sup>st</sup> Century Cures initiative is trying to attain.
- (4) Sec. 4004(b), p.251, line 16 requires institute directors to assess the money invested in a grant relative to the potential scientific discovery. Basic, discovery research is so named because no one knows the results of the experiment they are about to conduct. Furthermore, the potential scientific discovery may lead to other discoveries and developments years or decades in the future. It is not possible for anyone to accurately predict the outcomes of discovery research much less determine whether the financial investment is worthwhile given the long timeframes required for some discoveries to be used.
- (5) Sec. 4004(c) and (d) request the GAO to study waste, fraud and lack of consistency at the NIH as well as duplication in biomedical research. We support improving efficiencies at all federal agencies including the NIH. These studies should be completed before any legislative attempts are made to improve accountability at the NIH.

Our recommendation: Sec. 4004(b) should be removed in its entirety. We support Sec. 4004(c) and (d).

#### **Sec. 4007 – Additional funding for NIH Common Fund**

Our concern: This section authorizes more funding for the Common Fund. Without an increase to the overall NIH budget and concomitant increases to the budgets of all institutes and centers, a boost in the budget of the Common Fund will mean a reduction in the funding for other institutes and centers. This will mean that important investigator-initiated research will not be funded. Given the stagnant federal budget for research over the past ten years, reducing funding to any part of the NIH will harm research.

Our recommendation: Remove Sec. 4007.

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<sup>3</sup> Research!America. "America Speaks" vol. 14. <http://www.researchamerica.org/uploads/AmericaSpeaksV14.pdf>.



**Sec. 4008 – Additional funding for NIH brain research**

Our concern: This section authorizes more funding for the BRAIN initiative. The scientific research enterprise works at its best when undirected, investigator-initiated research is fully funded. Diverting resources to specified projects, such as the BRAIN initiative, detracts from the vibrance and productivity of the enterprise. We prefer a system where scientists compete for grants that are awarded based on exemplary, peer-reviewed grant applications.

Our recommendation: Remove Sec. 4008.



February 10, 2015

The Honorable Fred Upton  
Chairman  
Committee on Energy and Commerce  
2125 Rayburn House Office Building  
Washington, DC 20515

Dear Chairman Upton:

On behalf of over 52,000 members of the American Society of Anesthesiologists (ASA), I write to comment on the 21st Century Cures initiative discussion document and, specifically, to ask for consideration of National Institutes of Health (NIH) funding for the SmartTots research initiative. ASA applauds the Committee for its work culminated in the discussion draft. We recognize that the Committee has launched this initiative to accelerate discovery, development and delivery of new treatments to patients and appreciate the opportunity for stakeholders like ASA to provide input.

As Institute of Medicine-recognized leaders in patient safety, ASA recommends the inclusion of a provision in support of NIH pediatric anesthesia research when drafting final 21<sup>st</sup> Century Cures legislation. A public-private partnership between the FDA and the International Anesthesia Research Society (IARS), SmartTots, would be an appropriate entity through which NIH funding could prioritize pediatric anesthesia research efforts. Established with the purpose of funding research, SmartTots is a multi-year collaborative effort that aims to make surgery safer for the millions of infants and young children who undergo anesthesia and sedation each year. SmartTots research investigates the multiple facets of existing anesthetics and how they are administered to include dosage and exposure. Data collected from these studies will serve as a catalyst for the development of new practice guidelines and anesthetic drugs.

Concerns about the safety of anesthetic drugs for infants and young children initially arose when scientific studies in young animals showed that commonly used anesthetics can be harmful to the developing brain and result in adverse effects on behavior, learning, and memory. Accumulating evidence from studies in children suggests a similar association between surgery with anesthesia in early childhood and subsequent cognitive and behavioral abnormalities. Experts agree that additional preclinical and clinical research efforts are necessary; this research will help determine if particular anesthetic drugs are hazards to young children, to design the safest anesthetic regimens, to develop practice guidelines, and to potentially foster the development of new anesthetic drugs.

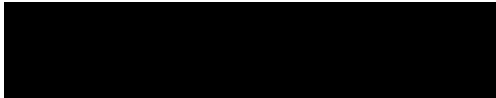
On November 19, 2014 the FDA Science Board held a meeting to review existing data related to the use and potential toxicity of anesthetics in the pediatric population. The FDA

Science Board's overall consensus was that there is a high likelihood that the troubling animal findings are translatable to humans. Funding for this research, including additional animal studies and definitive human clinical trials, is urgently needed.

SmartTots, through limited private funding, is already supporting research investigating the safety of pediatric anesthesia. Yet, a clinical trial is necessary to fully explore the complexities of this patient safety issue. An international steering committee, composed of members from the U.S., Australia, Europe, Canada, and Japan are in the process of designing a multi-center international trial, which will require major funding from government sources. The 21<sup>st</sup> Century Cures initiative is an important opportunity for Congress to support additional SmartTots research into the safety of anesthetic drugs in infants and children. We urge the Committee to take this into consideration when drafting final legislation.

Again, thank you for your support and dedication to the 21<sup>st</sup> Century Cures initiative. The American Society of Anesthesiologists appreciates this opportunity to comment. Please contact Nora Matus ([n.matus@asahq.org](mailto:n.matus@asahq.org)) at (202) 289-2222 with any questions the Committee may have.

Respectfully yours,

A black rectangular box redacting the signature of J.P. Abenstein.

J.P. Abenstein, M.S.E.E., M.D.  
President  
American Society of Anesthesiologists

February 10, 2015

The Honorable Fred Upton  
Chairman  
Committee on Energy and Commerce  
2125 Rayburn House Office Building  
Washington, D.C. 20515

The Honorable Diana DeGette  
Committee on Energy and Commerce  
2368 Rayburn House Office Building  
Washington, D.C. 20515

**Re: 21<sup>st</sup> Century Cures Discussion Draft Legislation**

Dear Chairman Upton and Congresswoman DeGette:

On behalf of the American Society of Nephrology (ASN) thank you for the opportunity to provide input to the Energy and Commerce Committee regarding the “21<sup>st</sup> Century Cures Act” discussion document. ASN commends the Committee for its commitment to accelerating the discovery, development, and delivery of promising new treatments to patients and stands ready to collaborate to achieve this important objective.

ASN, the world’s leading organization of kidney health professionals, represents more than 15,000 health professionals and scientists who are dedicated to treating and studying kidney disease and to improving the lives of the millions of patients it affects. ASN particularly supports efforts that bolster the ability of federal agencies and the American research and development enterprise to solve scientific challenges at every level from basic science through care delivery.

Kidney disease affects more than 20 million Americans. There are many unique causes of kidney disease, but when any type of kidney disease progresses to kidney failure, patients require either dialysis or transplantation to stay alive. Currently, 600,000 Americans have complete kidney failure, called end-stage renal disease (ESRD). Kidney disease disproportionately affects racial and ethnic minority populations, is associated with multiple co-morbidities including heart disease and diabetes, and is one of the most costly chronic conditions in the United States.

While America’s scientific leadership has yielded important treatments for some patients, others still wait because the state of biomedical research and innovation in certain diseases is not as advanced; kidney disease is among the conditions for which we must accelerate the pace of innovation.

Although people with kidney failure requiring dialysis (ESRD) comprise less than 1 percent of Medicare beneficiaries, they account for nearly 7 percent of Medicare’s budget: the Medicare ESRD Program is unique in that it covers every American with kidney failure regardless of age

or income. Yet despite these staggering costs, the fundamental principles of dialysis have not changed and patients with ESRD have seen only incremental improvements in their therapy in decades.

The 21st Century Cures initiative is a significant opportunity to spur research and facilitate development in kidney care and in other diseases where the state of biomedical research and therapies in certain diseases is not as advanced.

## **TITLE I—PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS**

### **SUBTITLE A—PATIENT FOCUSED DRUG DEVELOPMENT**

ASN applauds the Committee for prioritizing the inclusion of patient perspectives in the regulatory approval process. The society concurs that the meaningful incorporation of patient experiences into product development and regulatory decision making for medical products is an important objective. While ensuring the safety and effectiveness of medical products remains a paramount responsibility of the Food and Drug Administration (FDA), the FDA also supports the use of patient-reported outcomes (PRO) tools and patient preference metrics. However, the lack of clarity surrounding best practices for their development and application has resulted in slow adoption of these patient-centered tools.

Given that a patient's tolerance for risks will vary based on numerous factors including the severity of the disease or condition, the stage of the chronic disease, and the availability of alternative treatment options, a need truly exists for another set of tools that would allow regulators to better understand how affected patients would assess the overall benefits and risks associated with a product.

As proposed in the discussion draft, the experience of a patient living with a particular disease; the burden of living with or managing the disease; the impact of the disease on daily life and long-term functioning; the effect of current therapeutic options on different aspects of the disease; and patients' willingness to accept various levels of risk based upon potential benefit are all important considerations for a framework that would facilitate the incorporation of patients' experience data into regulatory decisions. ASN also supports the concept of convening workshops for patients, representatives from advocacy groups and disease research foundations, FDA staff, and methodological experts to provide input on the development of such a framework.

Reflective of ASN's commitment to facilitating the incorporation of patient preferences into the regulatory process, the society's public-private partnership with the Food and Drug Administration (the Kidney Health Initiative (KHI) mentioned under Title II Subtitle A of this letter) is confronting this topic. KHI's workshop (planned for the second half 2015) will engage kidney disease patients, in conjunction with regulators and industry, to understand their preferences and define future opportunities to develop tools that will assess benefit and risk of medical devices.

### **SUBTITLE B—SURROGATE ENDPOINT QUALIFICATION AND UTILIZATION**

ASN strongly supports the concept of establishing a predictable, transparent process for FDA's consideration, and possible qualification, of surrogate endpoints. In countless areas of medicine—including in the nephrology space—successfully completed large scale controlled

trials have failed to result in new approved products for patients. The reasons for these failures are complex and myriad, but one contributing factor is the lack of validated outcome measures and endpoints to feasibly assess success in many disease states.

For example, trials must reverse kidney failure or reduce deaths to gain approval for new treatments. As a consequence, these endpoints hinder the development of drugs that could potentially intervene earlier in the disease process and slow or halt progression to kidney failure because the trials would be too long and expensive to measure the results against the endpoints. Instead, most trials enroll patients who have already progressed to kidney failure.

The development of validated, robust surrogate endpoints and biomarkers—particularly early in the course of a disease—would accelerate discovery of new treatment and cures in nephrology and in other areas of medicine. The society strongly agrees with the proposal to consult with scientific experts and involve individuals with direct expertise in the relevant therapeutic areas, biostatistics, and pharmacogenetics, in the consideration of any surrogate endpoints or biomarkers to be utilized in regulatory decision-making.

### **SUBTITLE C—APPROVAL OF BREAKTHROUGH THERAPIES**

The current FDA Breakthrough Therapy Designation program is an important effort to date to reduce the time required to bring new drugs to market. ASN is supportive of FDA exploring expanding this effort to approval of drugs that have received breakthrough therapy designation under Section 506(a) of the Federal Food, Drug, and Cosmetic Act (FFDCA) when early stage clinical data provides sufficient evidence under the current safety and efficacy standards, considering the risks and benefits of the drug and the risks associated with the disease or condition for which unmet medical needs exist.

This provision of the draft legislation has the potential to help expedite novel therapies into patients' hands. However, ASN urges greater emphasis in the legislation regarding the consultation with, and role of scientists and other experts, representatives of patient advocacy organizations (including patients themselves) and disease research foundations, and other interested parties through a public process to ensure that regulatory efforts to meet this goal are conducted in the safest, most evidence-based manner.

### **Subtitle E—Priority Review for Breakthrough Devices**

Consistent with its support for providing faster access to new drugs, ASN also supports the concept of Medicare and Medicaid coverage of medical devices that have been reviewed and approved under an expedited review process by the FDA—provided, as noted in the discussion draft, that the standards for approval are the same or exceed the same approval standards for devices considered under the standard review process.

### **Subtitle N—Orphan Product Extensions Now**

ASN supports federal incentives to encourage industry investment in new therapies for complex diseases, including kidney disease, which is a broad term for dozens and dozens of diseases that affect kidney health and function. Many of these are relatively rare diseases, and consequently, many of the millions of Americans affected by one among this panoply of conditions have no therapeutic option. In lieu of treatment, some will progress to complete kidney failure. The FDA has approved fewer new therapies for kidney disease in the last 10

years than most major diseases. As such, incentives to promote investments in orphan products could be beneficial to patients.

#### **Subtitle O—Helping Young Emerging Scientists**

Investments in basic and clinical research are the foundation of future therapies and cures. Yet funding increases for the National Institutes of Health (NIH) have not kept pace with rising inflation, compromising our nation's ability to fund promising scientists. This trend is likely a contributing force behind the historic low application success rates and all-time high average age an investigator receives their first research grant.

Not surprisingly, these figures have a chilling effect on the number of young scientists choosing to dedicate their careers to medical research. As the brightest minds turn elsewhere, America's position as the global leader in research and innovation—and in bringing cures to patients—is compromised. ASN supports Congressional efforts to help young, emerging scientists gain a successful start to their research careers. Among these efforts, the society encourages Congress to consider expanding NIH loan repayment programs for MDs and PhDs as a way of promoting science careers, including in the kidney field.

#### **Subtitle P—Fostering High-Risk, High-Reward Science**

The NIH history of funding extramural, investigator-initiated grants has yielded unparalleled dividends in medical discoveries and cures. This successful model of research funding should be robustly and stably funded. However, there may be research funding models that complement this tradition, introducing a component of more high-risk—but high-reward—science to the NIH portfolio.

The private and philanthropic sectors have successfully been using prize competitions for years as a mechanism for spurring scientific and technologic breakthroughs in a number of fields. Unlike traditional research and development models, competitions have the added benefit that the prize is only paid out if a competitor wins, and the competitions also draw competitors from outside those traditionally interested in the space.

The 2007 America Creating Opportunities to Meaningfully Promote Excellence in Technology, Education, and Science Act of 2007 (also known as the America COMPETES Act) authorizing federal agencies to conduct prize competitions. ASN believes Congress should investigate dedicating funding towards prize competitions and other mechanisms that promote consideration of high-risk, high-reward science, especially in fields where innovation has been stagnant, including nephrology. However, the society emphasizes that such high-risk, high-reward science must not come at the expense of traditional research funding models, and that this approach to promoting innovation should be used only in certain, carefully considered situations.

### **TITLE II—BUILDING THE FOUNDATION FOR 21ST CENTURY MEDICINE, INCLUDING HELPING YOUNG SCIENTISTS**

#### **SUBTITLE A—21ST CENTURY CURES CONSORTIUM ACT**

ASN believes the proposal described in Section 2001 to establish a public-private partnership to accelerate the discovery, development, and delivery in the United States of innovative cures, treatments, and preventive measures for patients has substantial promise to assist in the

development and delivery of new therapies for patients. The society applauds the Committee for including the concept of the 21<sup>st</sup> Century Cures Consortium in the discussion draft, and offers insights from a similar, successful public-private partnership with the FDA.

To respond to the serious and under-recognized epidemic of kidney disease in the United States, the Food and Drug Administration and the American Society of Nephrology in 2012 founded the Kidney Health Initiative (KHI)—a public-private partnership designed to create a collaborative environment in which the FDA and the greater kidney community can interact to optimize the evaluation of drugs, devices, biologics, and food products. The mission of this public-private partnership between ASN and FDA is to advance scientific understanding of the kidney health and patient safety implications of new and existing medical products and to foster development of therapies for diseases that affect the kidney by creating a collaborative environment in which FDA and the greater nephrology community can interact to optimize evaluation of drugs, devices, biologics, and food products.

Similar to the proposed 21<sup>st</sup> Century Cures Consortium, the KHI membership and board of directors—which is co-chaired by an ASN member and an FDA staff person—includes the breadth of stakeholders, including patient, health professional, pharmaceutical, device, and dialysis company members, as well as the Centers for Medicare and Medicaid Services (CMS), FDA, and NIH.

Current projects, driven by multi-disciplinary workgroups, focus on the development of clinical trial endpoints, assessment of patient preferences in the approval of medical devices, data standards, value and utilization of pragmatic trials, and much more. With more than 70 members and nearly a dozen active projects tackling the barriers to innovation in kidney disease underway, ASN believes that the collaborative KHI approach to fostering innovation can serve as a model for other areas of medicine where scientific advancements are needed.

## **SUBTITLE B—MEDICAL PRODUCT INNOVATION ADVISORY COMMISSION**

ASN supports the creation of an independent Medical Product Innovation Advisory Commission based on MedPAC. MedPAC has served as a credible, authoritative voice on a variety of health and medical policy issues; its staff and committee members are highly knowledgeable and offer thoughtful insights on complex policy issues. ASN believes a similarly structured entity to advise Congress on issues related to the discovery-development-delivery cycle could help facilitate the innovation process and improve patient access to cures.

## **SUBTITLE H—COVERAGE WITH EVIDENCE DEVELOPMENT**

One of the frequently identified barriers to the development of new medical products is the siloed decision-making between the FDA and CMS. Although the missions of the two agencies are distinct and equally important, from an investment perspective, the possibility that FDA may approve a new medical product only to have CMS—at a much later date—rule unfavorably in terms of necessity or coverage can be a deterrent. This deterrent comes at a cost to patients who might otherwise benefit from a new drug or device on the market. Permitting Medicare beneficiaries to access products that are the subject of ongoing clinical trials would help reduce uncertainty for technology developers and simultaneously benefit patients. Considering the paucity of new therapies in the nephrology space compared to other areas of medicine, patients with kidney disease may stand to benefit significantly from any reduced disincentives to invest in a new product that Coverage with Evidence Development may provide.



ASN supports the concept of subtitle H as articulated in the discussion draft.

## **SUBTITLE F—FDA SUCCESSION PLANNING**

Facilitating the professional development and up-to-date scientific knowledge of federal agency staff is crucial to the success of every agency with a mission related to the public health of the United States.

National and international meetings play a critical role in the scientific process and in the implementation of scientific advances by allowing for analytical discussion and interaction between government experts and other physicians and scientists. Such interactions facilitate research and support the collaborative efforts between academia and federal agencies necessary to address serious public health threats and advance the discovery of life saving treatments and diagnostics. As medical and scientific innovation becomes more global, the information sharing, mentoring, and professional collaboration that occurs between U.S. scientists and their colleagues from around the world at these meetings becomes all the more paramount to maintain our nation's role as the leader in research, translational science, and innovation.

Ensuring a robust, well-trained pipeline of agency staff to ascend within agencies—as well as establishing contingency plans should planned staff transitions into key roles not occur—are fundamentally important to the function of federal agencies. Particularly in health care-related agencies, a deep understanding of the history of and nuances related to areas of responsibility is a necessity for developing and implementing or executing policies that affect the public health. As such, ASN commends the Committee's interest in succession planning and encourages the consideration of succession planning at other federal health care-related agencies—particularly CMS.

For example, although nearly 7 percent of Medicare's budget is allocated to the care of patients with kidney failure, CMS does not employ a single nephrologist on its staff of thousands. Although Medicare had nephrologists on staff in the past, the current dearth of nephrologists is problematic and could potentially have been avoided by a succession plan to account for this crucial staff expertise. The lack of internal knowledge regarding the vulnerable, costly kidney patient population creates challenges for the kidney community in communicating with CMS and impedes informed dialogue concerning the best possible policy decisions for patients.

As such, ASN also supports the most efficient possible review and approval processes for federal employees to travel to and participate in scientific conferences and meetings as recommended under Title IV Subtitle A Section 4003 of this letter.

## **SUBTITLE S—CONTINUING MEDICAL EDUCATION SUNSHINE EXEMPTION**

ASN support the provision outlined in Section 4381 that would clarify that peer-reviewed journals, journal reprints, journal supplements, and medical textbooks are excluded from the reporting requirement under the Sunshine Act.

## **TITLE II—BUILDING THE FOUNDATION FOR 21ST CENTURY MEDICINE, INCLUDING HELPING YOUNG SCIENTISTS**

### **SUBTITLE B—BROADER APPLICATION OF BAYESIAN STATISTICS AND ADAPTIVE TRIAL DESIGNS**

ASN supports the encouragement of the broader application of Bayesian statistics and adaptive trial designs. The topic of Bayesian statistics involves a number of technical issues, and the available methods are rapidly evolving; ASN would be pleased to provide input to Rep. Collins and his office as well as the Committee as this provision takes shape. In general, ASN believes that adaptive designs (Bayesian and non-Bayesian) are a useful new tool for conducting clinical trials efficiently. Hence, the society anticipates that the language in the bill will be helpful for research in many areas of medicine including kidney disease.

## **TITLE IV—ACCELERATING THE DISCOVERY, DEVELOPMENT, AND DELIVERY CYCLE AND CONTINUING 21ST CENTURY INNOVATION AT NIH, FDA, CDC, AND CMS**

### **SUBTITLE A—NATIONAL INSTITUTES OF HEALTH**

#### **Section 4001—NIH research strategic investment plan**

ASN supports the provision for NIH development of a Strategic Investment Plan. The society suggests that Congress consider encouraging NIH to examine the federal costs related to the care for each disease area when prioritizing research foci in such a planning effort. The society also believes NIH should seek input and feedback from stakeholders—particularly patients and scientific experts—throughout the planning process; this could easily be achieved by publication of notice in the Federal Register seeking public comments on draft plans.

#### **Section 4003—NIH travel**

While ASN recognizes the importance of reforms to prevent the abuse of federal funding for travel, recent travel bans and budget cuts are negatively affecting federal employee participation in scientific meetings and conferences. As noted above, their participation is critical for executing and advancing the mission of NIH, FDA, CMS and other federal public health agencies. Not only is participation in these meetings essential for the exchange of knowledge to advance science and medical care, it is also in many cases necessary for maintaining professional licenses for practicing medicine.

### **SUBTITLE I—TELEMEDICINE**

ASN commends the Committee for seeking input and feedback from stakeholders on telehealth as part of its larger 21<sup>st</sup> Century Cures initiative. The society concurs that telehealth has significant possibility to facilitate better access to care and holds great promise for improving the health and quality of life for patients nationwide.

While ASN believes that telehealth may increase access to care for some patients and help improve care transitions, the society is concerned that telehealth may (in some instances) be used as an inappropriate substitute for face-to-face visits, or may be used to provide unnecessary care. The society therefore suggests careful consideration of the scope of the initial program and urges implementation of rigorous testing—ideally in the form of a randomized controlled trial—to ensure that the program or pilots achieve the intended goals.

ASN believes that patients at every stage of kidney disease—from those with early-stage chronic kidney disease (CKD) who may be at risk to progressing, to those who are on dialysis, to those who have received a kidney transplant—may be uniquely poised to benefit from expansion of telehealth opportunities.

According to CMS, more than 51 percent of patients with kidney disease have 5 or more co-morbid conditions. Effective management of these co-morbidities is especially important for patients with earlier stages of kidney disease, during which proper care from a nephrologist can help slow the progression of kidney disease towards kidney failure as well as prevent the advancement of costly co-morbidities that are caused or worsened by kidney disease, such as hypertension. Besides improving patient outcomes, facilitating patient access to subspecialists may contribute to long term cost-savings—particularly to the Medicare ESRD Program by preventing people from requiring dialysis.

ASN supports the proposal to eliminate existing limitations on what qualifies as an originating site, including geographic limitations to rural Health Professional Shortage Areas or counties outside of a Metropolitan Statistical Area. In particular, the society supports permitting patients' homes to qualify as originating sites for the provision of telehealth services. Lifting these limitations would facilitate patient access to care, eliminating the need to travel to interface with their nephrology care team.

Home dialysis is an important treatment option that offers patients significant quality of life advantages, including clinically meaningful improvements in physical and mental health. The society encourages the Committee to designate the ESRD patient's home and dialysis facility as originating sites in statute. In doing so, the Committee would ensure access to this important treatment option for ESRD patients.

Both kidney transplant recipients and living kidney donors would also be well-served by expanded telehealth options. Kidney donor follow-up consultations, mandated by both Medicare and the United Network for Organ Sharing, typically comprise a simple well-patient visit for which donors must bear the costs of a day off work and travel; were patients' homes to be designed as originating site, many of these consultations could easily be provided via telehealth.

ASN strongly believes that rigorous testing to evaluate whether telehealth services are achieved their intended goals is imperative. The society suggests the use of limited trial runs in the manner of a randomized clinical trial: one group of Medicare patients is allowed to receive care via telehealth while another highly similar group is restricted to presently-available face-to-face interactions. Pre-specified patient outcomes and cost metrics would be analyzed and the cost savings/readmissions-preventing hypothesis verified in close to real-time. Although there is wide consensus that telehealth has the potential to improve patient access, reduce hospitalizations, and reduce costs, these hypotheses remain unproven and therefore must be closely evaluated.

### **Additional Recommendations for Inclusion in the 21<sup>st</sup> Century Bill**

#### **Establishment of a Single NIH Institutional Review Board for Multi-Site Studies**

ASN supports the establishment of a single NIH Institutional Review Board (IRB) for multi-site studies. While IRBs assure that appropriate steps are taken to protect the rights and welfare of clinical trial participants, review of a multi-site study by the IRB of each participating site involves significant administrative burden in terms of IRB staff and members' time to perform duplicative reviews.

When each participating institution's IRB conducts a review, the process can take many months and significantly delay the initiation of research and patient recruitment for clinical trials. Use of

single IRBs in multi-site studies, on the other hand, has been shown to decrease approval times for clinical protocols and may be more cost effective than local IRB review.

### **Online Resources for Patients to Find and Enroll in Clinical Trials**

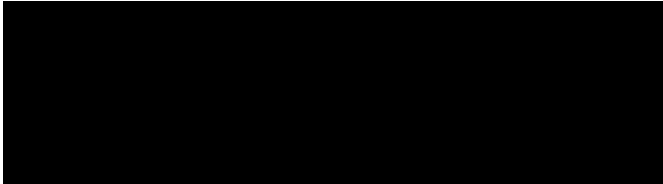
Patient recruitment for clinical trials is a significant barrier to new drug and device development in many areas of medicine, and is a particular challenge in the nephrology space due to the heterogeneity of kidney diseases and the high rate of co-morbid conditions among kidney patients. Without sufficient patient recruitment, industry cannot bring new therapies to market; many kidney studies languish for lack of volunteers. As such, ASN recommends the Committee consider the development of an online clinical trial enrollment resource to help connect patients with relevant studies. The Lung-MAP (<http://www.lung-map.org/>), an online tool developed in part by the National Cancer Institute, may serve as a model to help build patient awareness of clinical trials and match them with the most appropriate study.

### **Conclusion**

ASN applauds the Committee for its work on this initiative and its commitment to ensuring that the United States continues its preeminence in the discovery, development, and delivery cycle and thus, remains the world leader in innovation. The society is grateful for the opportunity to provide on the discussion draft and hopes this feedback is helpful.

Again, thank you for your time and consideration. To discuss ASN's input please contact ASN Manager of Policy and Government Affairs Rachel Meyer at [meyer@asn-online.org](mailto:meyer@asn-online.org) or at (202) 640-4659.

Sincerely,



John R. Sedor, MD, FASN  
Chair, Public Policy Board  
Secretary-Treasurer



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February 12, 2015

The Honorable Fred Upton  
Chairman  
Energy and Commerce Committee  
U.S. House of Representatives  
Washington, DC 20515

The Honorable Frank Pallone  
Ranking Member  
Energy and Commerce Committee  
U.S. House of Representatives  
Washington, DC 20515

Dear Chairman Upton and Ranking Member Pallone:

On behalf of the American Thoracic Society (ATS), thank you for the opportunity to comment on the committee's 21<sup>st</sup> Century Cures legislation. The ATS is a 15,000 member scientific medical organization dedicated to the prevention, detection, treatment and cure of respiratory disease, critical care illness and sleep related disorders through research, clinical care and advocacy. The ATS focuses on respiratory health issues including tobacco cessation, chronic obstructive pulmonary disease (COPD), critical illness, tuberculosis and sleep-disordered breathing.

#### General Comments

The ATS has reviewed the available sections of the draft 21<sup>st</sup> Century Cures legislation and we believe that there are a number of proposals in the legislation that would help accelerate research and development. The ATS is particularly pleased to note inclusion of the Antibiotic Development to Advance Patient Treatment Act (ADAPT) that would encourage new drug approval and support the pipeline of young investigators. There are other sections of the bill we are also encouraged by.

We must note, however, the primary deficiency in the bill is that it does not address the biggest road block to scientific advancement – NIH funding. If we truly aim to accelerate treatments and cures, funding for the NIH, our nation's main biomedical research institution supporting basic, clinical and translation science, needs and increased sustained investment.

The ATS notes with some concern the number of important provisions for which legislative language has not yet been shared with the community.

Without reviewing the legislative text for important sections it is difficult to give thoughtful feedback on this important legislation. N. Several key sections of the bill, like: Section 1082-CMS coverage of breakthrough devices; Subtitle H—Facilitating Responsible Communication of Scientific and Medical Developments; Subtitle J—Modernizing Regulation of Diagnostics; Subtitle K—Interoperability; Subtitle Q—Precision Medicine; Subtitle E—FDA Hiring, Travel, and Training; have not yet been shared with the community.

The ATS commends the Committee for incorporating the patient perspective in the regulatory process. We recommend that where federal agency advisory panels exist or are newly-created that patient representatives be included as well as in all facets of the drug development process continuum. We have the following additional comments on the legislation:

#### **Subtitle A – Patient Focused Drug Development**

The ATS supports the intent of establishing a framework for FDA for “meaningful incorporation of patient experience data.” We urge the committee to include patient representatives in a triangular approach in drug development with regulatory bodies and industry from early in the development process until the end.

#### **Subtitle D – Antibiotic Drug Development**

The ATS strongly supports the ADAPT Act as included in Sections 1061 – 1063. Our members are often the primary physicians caring for patients with multi-drug resistant (MDR) bacterial infections as they present to the critical care unit or develop infectious complications after admission for other acute illnesses. These include pneumonia, one of the most common and the most lethal type of infection caused by MDR bacteria, drug resistant sepsis infections and drug resistant tuberculosis (TB).

The Centers for Disease Control and Prevention (CDC) identified drug resistant TB as a serious threat to public health in its report, *Antibiotic Resistance Threats in the United States, 2013*. The treatment regimen for multi-drug resistant (MDR)-TB is a long and arduous two years, using drugs with severe side effects such as hearing loss and psychosis. The difficulty of these long treatments often results in patient dropout from treatment, which increases the risk of development of antibiotic resistance to the incomplete course of therapy. New antibiotic drugs are urgently needed to prevent and treat drug resistant TB and other resistant infections. The ADAPT ACT will help speed the development and Food and Drug Administration (FDA) approval of new drugs and biological products for use in limited populations of patients to address increases in bacterial resistance.

#### **Subtitle F – Accelerated Approval for Breakthrough Devices**

The ATS supports this measure to create an accelerated FDA approval pathway for medical devices. Many in our patient population of people with respiratory diseases such as COPD and cystic fibrosis rely on medical devices for treatment and management of their conditions. As innovative new technologies are developed, FDA should have similarly expedited approval pathways for breakthrough medical devices, particularly those that address unmet medical needs.

### **Subtitle G: Expanded Access**

The ATS supports the addition of transparency requirements for expanded access programs for drugs not yet approved by FDA as well as the creation of an expanded access task force to provide further recommendations to Congress regarding further reforms of the program. The ATS recommends that patient representatives and practicing physicians be part of the task force.

### **Subtitles K & L – Cures Acceleration Network & Dormant Therapies**

The ATS supports this measure although we recommend further clarification on a sustainable funding stream to ensure that the National Center for Advancing Translational Sciences (NCATS) can advance this research to find new uses for off-patent drugs. Similarly, the ATS supports the MODDERN Cures Act measure that would encourage research and development of new therapies for scientifically complex chronic diseases and rare diseases.

### **Title II, Subtitle N – 21<sup>st</sup> Century Cures Chronic Disease Initiative Act**

With the growing aging population in the U.S., including many people with multiple complex chronic illnesses, there is a serious need for more research, including longitudinal studies, on diagnosis, treatment and prevention of chronic disease. Better system-wide management of chronic diseases, like COPD, asthma, sleep-disordered breathing and other chronic respiratory conditions will improve public health and reduce health system costs. While the idea of an initiative on chronic disease is of great interest to the ATS, we would recommend that this proposal be clarified and expanded on to facilitate multiple longitudinal studies on chronic diseases with the highest public health impact, including COPD, the third leading cause of death in the U.S.

### **Subtitle O – Helping Emerging Young Scientists**

The ATS supports this proposal to assist emerging young scientists. We are very concerned that due to federal funding cuts to biomedical research and training there is a lack of opportunities for young investigators and many are choosing alternate career paths as a result. Young investigators, including physician-scientists, represent the future of scientific innovation and we must act now to sustain this pipeline. We urge the committee to allocate a portion of the funds for this initiative to support physician-scientists, and additionally to modify the current language limiting program eligibility to 15 years after completing fellowship for physician-scientists.

### **Subtitle P – Fostering High-Risk, High-Reward Science**

We urge the committee to clarify and define “high-risk, high-reward science” and how this will be applied to disease areas. Additionally, we urge the committee to include basic/discovery science in this initiative to promote research into new discoveries across biomedical research.

### **Title III, Subtitle A – Clinical Research Modernization Act**

The ATS supports this measure to streamline the institutional review board (IRB) process and utilize single/shared IRB’s for multi-institutional studies to minimize administrative burden.

### **Subtitles D & E – Pediatric Research**

The ATS supports the implementation of the National Pediatric Research Network and the Global Pediatric Clinical Trial Network as mechanisms to expand research on child health. This initiative is especially critical since many children suffer from rare diseases that require larger networks for effective trials.

### **Title IV, Subtitle A – NIH Strategic Plan**

The ATS believes that development of a strategic plan across NIH could be beneficial, with some reservations. We are pleased to note the reservation of at least 55% of NIH funding for basic science research, although we believe this requirement should be reviewed annually to ensure appropriate opportunity to respond to advances within basic, clinical or translational science. We thank the committee for prioritizing pediatric and rare disease research the strategic plan.

The plan's strategic focus areas should include a thoughtful consideration of the impact of past resources investments into specific disease areas that have had major public health impact, such as in cardiovascular diseases – and how these successes can be replicated in other highly prevalent diseases, such as respiratory diseases. We do have a concern that biannual reviews of the plan could increase administrative costs in the Office of the NIH Director, reducing already limited funds available for research.

### **Section 4002 – Biomedical Research Working Group**

The ATS supports the intent of this section to create a working group to study and make recommendations on reducing administrative burdens on researchers, although we recommend some clarification and modification on appointments to the working group. We recommend that fewer member of the group be political appointees and that there is more peer input from the scientific and medical communities on the member selection process. We also recommend that patient representatives be part of this working group.

### **Section 4003 – NIH Travel**

We note the placeholder for a provision on NIH travel. The ATS has found that travel requirements and restrictions placed on NIH and other federal agency staff over the past few years have served to impede the free flow of scientific information, including research, between medical societies, such as the ATS and federal agencies for which this information is critical for advancing research and ultimately public health. Agency staff participation in scientific meetings and workshops where basic, clinical and translational scientific research findings are presented and discussed is essential to inform NIH institutes and help guide determination of research priorities. Denying or restricting NIH staff of the opportunities to participate in these meetings places additional burdens on both NIH staff and investigators to find other opportunities to hold these important discussions. The ATS urges the committee to remove harmful restrictions on NIH staff travel. The ATS further recommends Congress consider policy that would allow for scientists across federal agency to more freely participate in scientific meetings and conferences.



#### **Section 4004 – Increasing Accountability at the NIH**

The ATS has serious reservations about this provision, which we believe could potentially dilute and even subvert the scientific peer review process by giving institute directors the ability to unilaterally and independently review every research grant that has already gone through an extensive peer review process through the institute's advisory council and reject it. Institute directors have the opportunity to review and express their recommendation on individual grants through their position on advisory councils. An additional layer of director review following institute advisory council decision is unnecessary. This proposal would damage the integrity of the peer review process and we urge the committee to eliminate this provision.

#### **Subtitle O – Accelerating Innovation in Medicine**

The ATS would support the establishment of a program that allows patients access to medical device treatments sooner than would otherwise be available. The ATS would caution against devices being voluntarily excluded from coverage; therefore, requiring payment for these experimental devices to fall solely on the patient as this could mean that all patients who could benefit from the potentially life-saving technology would not have access.

#### **Subtitle R – Advancing Care for Exceptional Kids**

The ATS supports this provision to create a Medicaid and CHIP Care Coordination program for children with complex medical conditions. Children and adolescents with respiratory diseases such as cystic fibrosis and interstitial lung disease have significant and complex therapeutic and ancillary service needs, but for too many, these critical services are not continuously available due to financial barriers, shortages of providers and other barriers. We urge the committee and the Congress to provide adequate funding so that all children in need of this essential care coordination receive it.

#### **Subtitle S – Continuing Medical Education Sunshine Exemptions**

The ATS strongly supports this provision would exclude scientific journals and reprints and medical textbooks from reporting requirements under the Sunshine Act. The requirement to document and report on journal reprints is imposing a significant administrative burden on medical societies such as the ATS. We thank the committee for including this important provision to reduce administrative burdens in the 21<sup>st</sup> Century Cures legislation.

#### **Section 5068 – FDA Advisory Committee process**


Where patient representatives are included, such as on FDA advisory panels, the ATS recommends that patients have voting rights on those panels (as patient representatives cannot currently vote when they serve on FDA advisory panels).

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The ATS thanks the committee for the opportunity to comment. If you have any questions, please Contact Nuala Moore, Associate Director of Government Relations at 202.296.9770 or [Nmoore@thoracic.org](mailto:Nmoore@thoracic.org).

Sincerely,



Tom Ferkol, M.D.  
President  
American Thoracic Society

## **Amgen Comments on “21<sup>st</sup> Century Cures” Discussion Document\***

*\*Discussion Draft Stamped: F:\WPB\CO14R\CURES\CONSOLIDATED -- January 26, 2015 (5:26 p.m.)*

Amgen appreciates the opportunity to continue working with you on the “21st Century Cures” initiative. The transparent and open process for stakeholder feedback you have established is truly impressive and we look forward to continuing to serve as a resource to you as this process moves forward. We all share the same goal of ensuring that the drug regulatory framework keeps pace with advances in medical innovation so that patients can ultimately benefit from more treatments.

We offer below several comments on your recently released discussion draft. While we have not provided comment on every provision, we will continue to review the draft as a whole and provide further feedback as it is developed or requested. We are also continuing to work with our industry trade associations to consolidate feedback.

Overall, your draft contains many important provisions that can meaningfully improve the discovery, development, and delivery of new medical products. Along with these improvements, it is important to continue to be mindful of the inherent tension that exists between new requirements placed on the Agency and how they could impact the current FDA review model by re-directing Agency resources. While individual provisions may clearly improve the system, ultimately, the legislation will have to be weighed by the sum of its parts in terms of the impact on the Agency in its continued ability to focus on reviewing new treatments for patients. We know you understand this paradigm well and we all want to see FDA have the resources necessary to update regulations while maintaining a strong focus on new product reviews.

Thank you again for your work on this important initiative and please let us know if you have any questions.

### **Comments:**

#### **Title I, Subtitle G – Expanded Access**

- Amgen has made publically available our policy on expanded access including the criteria used for considering requests for expanded access as well as the process for making such requests.<sup>1</sup> As this issue moves forward we will want to ensure that drug manufacturers are able to preserve their judgment regarding the appropriateness of providing investigational drug to a particular patient. In addition, it is important to ensure that regulations around expanded access not

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have the unintended consequence of patients being unwilling to join (or continue on) clinical studies in favor of receiving investigational drug through the expanded access process. This would have an adverse impact on registration studies and slow progress towards product approval and also impair a company's ability to deliver on post-marketing commitments. With respect to the specific language in the bill, a few comments:

- With respect to manufacturers making publicly available their expanded access policy, it would be more efficient (including for updating) if this were done through a manufacturer's website rather than having to provide their policy to HHS.
- The amount of detail in explanation for denying request could cause debate and open the manufacturer's judgment to be second-guessed by others. There could be many valid reasons for not providing access to an investigational drug, some of which the requestor may not fully appreciate and also could be considered confidential commercial information.
- With respect to the GAO report, it is unclear how the GAO would gain access to data on number of expanded access requests denied by sponsors/manufacturers. This could potentially place additional burden on sponsors to track and report the information that the GAO would need to support its reports.
- Support establishing an Expanded Access Task Force if it would help to simplify and clarify the process, including looking at the existing FDA regulations and guidance.
- Support finalizing the FDA draft guidance and Q&A as written.

#### **Title I, Subtitle H – Facilitating Responsible Communication of Scientific and Medical Developments**

- We understand that you are still working on a proposal to clarify the types of communication that drug and device developers can share with physicians, insurers, and researchers. We look forward to reviewing your proposal. As you continue your work in this area we have attached the proposal that we previously shared which focuses on improving one aspect of the healthcare communication issue which is dissemination of health care economic information to payers, formulary committees, or other similar entities.<sup>2</sup>

In 1997, Congress passed Section 114 of the Food and Drug Modernization Act of 1997 (FDAMA 114), which permits drug manufacturers to disseminate health

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<sup>2</sup> See attachment titled "Amgen 21<sup>st</sup> Century Cures Proposal – FDAMA 114"

care economic information that is directly related to an approved indication to payers, formulary committees, or other similar entities so long as it is based on “competent and reliable scientific evidence.” Although the intent of Congress in enacting FDAMA 114 was to ensure that these entities have the economic information necessary to make decisions regarding the coverage, reimbursement, and selection of drugs, manufacturers have been stifled from disseminating important information about the value of their products because key terms in the statutory provision are undefined and FDA has yet to issue guidance interpreting these terms.

The proposal we offer attempts to remedy the current statutory ambiguity and to facilitate appropriate dissemination of economically and clinically relevant information to payers, formulary committees, or other similar entities. Such information would facilitate important conversations between payers and manufacturers about the economic consequences and value of new and existing biopharmaceutical products, which are necessary to move toward a value-based health care delivery system. Notably, this legislative proposal in no way changes or otherwise affects FDA’s approval and regulation of biopharmaceutical products.

#### **Title I, Subtitle I – Modernizing the Regulation of Social Media**

- We support the draft language regarding the regulation of communication on social media.

#### **Title I, Subtitle J – Streamlined Data Review**

- Page 95; line 24 – Suggest removing the presumption that full data sets should be submitted. The current language implies that the default requirement is the submission of the full data set unless otherwise specified by the Secretary. If a summary review is being done then the full data sets should not be required, however, the full data sets can still be provided if requested.

#### **Title II, Subtitle E – Sensible Oversight for Technology Which Advances Regulatory Efficiency**

- We support the exclusion of “health software” from device regulations and also support the addition of categories of software that allow patient self-management of medications and captures patient-reported outcomes data for use by a health practitioner.

## **Title II, Subtitle H – Coverage With Evidence Development**

- Although the full title of the section (*Authority for CED for Medical Devices under the Medicare Program*) suggests the intent of the provision is to address coverage for devices, as currently written, the provision would not be limited to devices and would also apply to drugs and biologicals. Codifying CED for drugs and biologics is not necessary as the current statute already supports coverage of drugs and biologicals for their medically accepted indications. Therefore, we recommend this provision be revised to focus on coverage mechanisms specific to devices. We further recommend the Committee do so outside of the CED framework to avoid confusion with CMS guidance on CED.

## **Title II, Subtitle I – Combination Products**

- Reform in the area of combination products is welcome in order to prevent delays in overall development timelines as well as delays in the regulatory review of combination product applications. We have previously submitted a proposal in this area and believe those ideas can still be useful as you continue to work on this issue.<sup>3</sup> With respect to the current bill draft we offer the following comments:
  - P 198, line 17-20 – While having the agency center with primary jurisdiction as the sole point of contact for the sponsor may be beneficial for later stages of development and filing, it may hinder interactions in the early development stages and prevent collaboration opportunities. There is technical information that biopharmaceutical companies need to receive and communicate to the device center (CDRH), solely on the device constituent part of their combination product. This section of the bill appears to disallow that access point. Current CDRH guidance<sup>4</sup> already allows for this interaction and it would be helpful for the drug center (CDER) to recognize and follow this guidance.
  - Page 198, line 20-22 – The bill provides that the Office of Combination Products (OCP) will act as the coordinator for communications during premarket review, and this is a concern because OCP is not staffed to do this. OCP should be copied on communications for awareness and to ensure that they can ensure consistency and timeliness, but they should not lead or coordinate the communication / consultation process. This should

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<sup>3</sup> See attachment titled “Amgen 21 Century Cures Proposal -- Improving Combination Product Regulation”

<sup>4</sup> [Guidance for Industry and FDA Staff: Requests for Feedback on Medical Device Submissions – The Pre-Submission Program and Meetings with Food and Drug Administration Staff (CDRH/CBER, February 2014; <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf>)]

be the role of the Agency center that is primary and they should be staffed with project management support to ensure this happens effectively and with transparency. FDA IT/IS (database/tracking efforts) should ensure that the consultancy review process (bi-directional) is transparent to all Centers and OCP, with electronic track/trace notifications for alerts regarding review timelines.

- Page 199, lines 1-2 – The scope of this section states that it deals with “premarket review.” If this term includes early collaboration review meetings, then agree with use of the term. If not, scope should be expanded to earlier reviews that discuss development plans (before premarket review of the submissions).
- Page 199, lines 3-6 – This section deals with OCP ensuring complete engagement of all centers in review meetings. However, engagement isn’t just attendance. Engagement includes review of the briefing document, participation in the pre-meeting cross-Center reviews, and speaking up in meetings with the non-Lead Center area of expertise. The Lead Center should be staffed sufficiently and be accountable for ensuring appropriate meeting attendance/participation since they should have full accountability for the applications and need to ‘own’ the process for the meetings being effective. OCP should be empowered to publish annual accountability metrics on how well the Centers did in this area.
- Page 199, lines 15-18 --- This section deals with the consulting agency center complying with guidance, regulations, policies. There should be a requirement that guidance, regulations, policies for combination products are followed by all review Centers (lead and consulting). Compliance should not be limited to just the roles/responsibilities and should include all combination product guidance, regulations, and policies for combination products.
- Page 201, lines 9-16 -- Suggest including early development engagement which may be pre-investigational in the definitions of “premarket review” and “reviews” so there is accountability throughout the development and review.
- Page 203, lines 14-21 – Suggest expanding this section to include determinations for simulated use vs. clinical trial data for indications (home use) and performance attributes (complete injection delivery in clinical bridging studies). This may include least burdensome text and still very good to focus questions on IFU and HF.

## **Title IV, Subtitle J – Revise IPPS New Technology Add-On Payment Reimbursement Amounts**

- We support the creation of a process to appeal NTAP denials in section 4201(a), but recommend several revisions to the proposal:
  - The legislative language should make clear that the NTAP applicant is the only entity that can seek this administrative review.
  - The legislative language should clarify the adjudicator of NTAP appeals will be the HHS Department of Appeals Board. The HHS Department of Appeals Board provides independent review of disputed decisions in a wide range of HHS programs, including administrative review of claims for entitlement to Medicare and individual claims for Medicare coverage and payment filed by beneficiaries or health care providers/suppliers.
  - NTAP applicants should have the right to seek judicial review if dissatisfied with administrative review.
  - The Secretary should be required to review NTAP decisions for FY 2016 and later fiscal years. The current discussion draft focuses on discharges as the triggering event and that does not appear to be appropriate given that this provision pertains to NTAP application denials.
- Section 4201 (b) would replace Healthcare Common Procedure Coding System (HCPCS) codes with National Drug Codes (NDC) for drugs and biologicals billed under Medicare Part B, presumably to shorten the timeframe for issuance of codes for new products. The draft legislation also includes language that addresses payment for Part B covered drugs and biologicals under the proposed NDC coding mechanism.

Concerns: HCPCS codes have long been used to bill physician-administered drugs under the medical benefit, whereas NDCs have been used in retail pharmacy transactions under the pharmacy benefit. There are significance differences between the codes sets, as well as the medical benefit vs. pharmacy benefit claims systems. This proposal to replace HCPCS codes with NDCs has numerous logistical and implementation issues and would be burdensome for providers and payers alike. Key issues include:

- Unclear Billing Amount: Unlike HCPCS codes, NDCs provide no mechanism for billing for doses that are less than the amount represented by the NDC. Providers commonly need to bill for less than the NDC amount and this proposal does not make it possible to appropriately bill for products in multi-dose vials.
- Inability to Identify NDCs: For products that are supplied in multi-packs, providers may not have systems in place that track the NDC once the packs are opened and separated, creating a risk that an incorrect NDC would be reported.
- Inconsistent with HIPAA Transaction Standards: Under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), HHS has



adopted HCPCS codes as the standard code set for billing for physician-administered drugs for all payers, including CMS, state Medicaid agencies, and private payers. This legislative proposal would appear to change the standard code set for Medicare Part B only. The repercussions for other payers are unclear. In addition, HIPAA requires a consensus-building process, including rulemaking, to change standard code sets. This proposal would short circuit the HIPAA requirement to build stakeholder consensus before changing a code set.

- Provider Billing System Limitations: It would be burdensome for virtually all providers to implement as their billing systems would need to be reconfigured from five-digit HCPCS codes to eleven-digit NDCs. Furthermore, providers would be forced to use NDCs for their Medicare claims, but HCPCS for claims submitted to other payers.
- CMS and Private Payer Administrative Concerns: Similarly, it would also be burdensome for CMS to implement and manage as the agency would have to create payment rates for significantly more codes than they currently do and would also need to reconfigure their claims processing systems and forms to accommodate NDCs. There would be an additional burden to keep the Medicare data set current as NDC codes can be changed or newly issued frequently. Private payers would be required by HIPAA to continue to use HCPCS codes, yet CMS would no longer issue or maintain HCPCS codes for drugs and biologicals.
- No Impact on Time to Establish ASP: This proposal would have no impact on speeding the ASP rate-setting process, as CMS would still need sales data, submitted by the manufacturer quarterly, to establish ASP payment rates.
- Statute on Average Sales Price: The proposal opens up the part of the Medicare statute that addresses Part B drug and biological payment (*i.e.*, Average Sales Price or ASP), which is not necessary to address timeliness for issuance of new codes.

Recommendation: A better policy solution to achieve timely issuance of Part B drug and biological billing codes would be to require CMS to issue HCPCS codes on a rolling or quarterly basis after drug and biological products are approved. CMS has a proven track record issuing HCPCS codes quarterly for use in other settings.

#### **Title IV, Subtitle S – Continuing Medical Education Sunshine Exemption**

- Generally support excluding peer-reviewed journals, journal reprints, journal supplements, and medical textbooks from the reporting requirement under the Sunshine Act. However, regarding terminology, the term “continuing medical education” has a specific meaning and refers to those symposia attended by health care providers that may have industry support. The proposed insert of new clause (xiii) (page 344, line 24) seems to have a broader purpose along lines of intending to capture anything that could be used for physician education. Suggest considering revising terminology so as to mitigate the risk of confusion.

## **Title V, Subtitle B – 21<sup>st</sup> Century Manufacturing**

- We are supportive of ensuring a continued dialogue with the FDA on novel manufacturing techniques and new technology. The proposed language in Section 5021 (page 349) is very broad and may benefit from inclusion of specific provisions illustrating the type of concepts which may help speed up the development of new medical products. With this mind, we've attached a document outlining such a proposal which we've shared with you previously.<sup>5</sup>

In addition, it should be noted that a one year requirement for putting out final guidance in this area of novel approaches and technologies is likely not feasible. It may be more beneficial to set up a process for a public meeting and proposed rule in order for the Agency to solicit input and receive detailed feedback from stakeholders. This would help alleviate the sole burden on the Agency to come up with proposals and also ensure stakeholders are able to share with the Agency detailed suggestions around novel ideas and approaches.

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<sup>5</sup> See attachment titled "Amgen 21<sup>st</sup> Century Cures – Early Clinical Development Proposal"

## **Amgen Comments on “21<sup>st</sup> Century Cures” Discussion Document\***

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<sup>2</sup> See attachment titled "Amgen 21<sup>st</sup> Century Cures Proposal – FDAMA 114"

care economic information that is directly related to an approved indication to payers, formulary committees, or other similar entities so long as it is based on “competent and reliable scientific evidence.” Although the intent of Congress in enacting FDAMA 114 was to ensure that these entities have the economic information necessary to make decisions regarding the coverage, reimbursement, and selection of drugs, manufacturers have been stifled from disseminating important information about the value of their products because key terms in the statutory provision are undefined and FDA has yet to issue guidance interpreting these terms.

The proposal we offer attempts to remedy the current statutory ambiguity and to facilitate appropriate dissemination of economically and clinically relevant information to payers, formulary committees, or other similar entities. Such information would facilitate important conversations between payers and manufacturers about the economic consequences and value of new and existing biopharmaceutical products, which are necessary to move toward a value-based health care delivery system. Notably, this legislative proposal in no way changes or otherwise affects FDA’s approval and regulation of biopharmaceutical products.

#### **Title I, Subtitle I – Modernizing the Regulation of Social Media**

- We support the draft language regarding the regulation of communication on social media.

#### **Title I, Subtitle J – Streamlined Data Review**

- Page 95; line 24 – Suggest removing the presumption that full data sets should be submitted. The current language implies that the default requirement is the submission of the full data set unless otherwise specified by the Secretary. If a summary review is being done then the full data sets should not be required, however, the full data sets can still be provided if requested.

#### **Title II, Subtitle E – Sensible Oversight for Technology Which Advances Regulatory Efficiency**

- We support the exclusion of “health software” from device regulations and also support the addition of categories of software that allow patient self-management of medications and captures patient-reported outcomes data for use by a health practitioner.

## **Title II, Subtitle H – Coverage With Evidence Development**

- Although the full title of the section (*Authority for CED for Medical Devices under the Medicare Program*) suggests the intent of the provision is to address coverage for devices, as currently written, the provision would not be limited to devices and would also apply to drugs and biologicals. Codifying CED for drugs and biologics is not necessary as the current statute already supports coverage of drugs and biologicals for their medically accepted indications. Therefore, we recommend this provision be revised to focus on coverage mechanisms specific to devices. We further recommend the Committee do so outside of the CED framework to avoid confusion with CMS guidance on CED.

## **Title II, Subtitle I – Combination Products**

- Reform in the area of combination products is welcome in order to prevent delays in overall development timelines as well as delays in the regulatory review of combination product applications. We have previously submitted a proposal in this area and believe those ideas can still be useful as you continue to work on this issue.<sup>3</sup> With respect to the current bill draft we offer the following comments:
  - P 198, line 17-20 – While having the agency center with primary jurisdiction as the sole point of contact for the sponsor may be beneficial for later stages of development and filing, it may hinder interactions in the early development stages and prevent collaboration opportunities. There is technical information that biopharmaceutical companies need to receive and communicate to the device center (CDRH), solely on the device constituent part of their combination product. This section of the bill appears to disallow that access point. Current CDRH guidance<sup>4</sup> already allows for this interaction and it would be helpful for the drug center (CDER) to recognize and follow this guidance.
  - Page 198, line 20-22 – The bill provides that the Office of Combination Products (OCP) will act as the coordinator for communications during premarket review, and this is a concern because OCP is not staffed to do this. OCP should be copied on communications for awareness and to ensure that they can ensure consistency and timeliness, but they should not lead or coordinate the communication / consultation process. This should

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<sup>3</sup> See attachment titled “Amgen 21 Century Cures Proposal -- Improving Combination Product Regulation”

<sup>4</sup> [Guidance for Industry and FDA Staff: Requests for Feedback on Medical Device Submissions – The Pre-Submission Program and Meetings with Food and Drug Administration Staff (CDRH/CBER, February 2014; <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf>)]

be the role of the Agency center that is primary and they should be staffed with project management support to ensure this happens effectively and with transparency. FDA IT/IS (database/tracking efforts) should ensure that the consultancy review process (bi-directional) is transparent to all Centers and OCP, with electronic track/trace notifications for alerts regarding review timelines.

- Page 199, lines 1-2 – The scope of this section states that it deals with “premarket review.” If this term includes early collaboration review meetings, then agree with use of the term. If not, scope should be expanded to earlier reviews that discuss development plans (before premarket review of the submissions).
- Page 199, lines 3-6 – This section deals with OCP ensuring complete engagement of all centers in review meetings. However, engagement isn’t just attendance. Engagement includes review of the briefing document, participation in the pre-meeting cross-Center reviews, and speaking up in meetings with the non-Lead Center area of expertise. The Lead Center should be staffed sufficiently and be accountable for ensuring appropriate meeting attendance/participation since they should have full accountability for the applications and need to ‘own’ the process for the meetings being effective. OCP should be empowered to publish annual accountability metrics on how well the Centers did in this area.
- Page 199, lines 15-18 --- This section deals with the consulting agency center complying with guidance, regulations, policies. There should be a requirement that guidance, regulations, policies for combination products are followed by all review Centers (lead and consulting). Compliance should not be limited to just the roles/responsibilities and should include all combination product guidance, regulations, and policies for combination products.
- Page 201, lines 9-16 -- Suggest including early development engagement which may be pre-investigational in the definitions of “premarket review” and “reviews” so there is accountability throughout the development and review.
- Page 203, lines 14-21 – Suggest expanding this section to include determinations for simulated use vs. clinical trial data for indications (home use) and performance attributes (complete injection delivery in clinical bridging studies). This may include least burdensome text and still very good to focus questions on IFU and HF.

**Title IV, Subtitle J – Revise IPPS New Technology Add-On Payment  
Reimbursement Amounts**

- We support the creation of a process to appeal NTAP denials in section 4201(a), but recommend several revisions to the proposal:
  - The legislative language should make clear that the NTAP applicant is the only entity that can seek this administrative review.
  - The legislative language should clarify the adjudicator of NTAP appeals will be the HHS Department of Appeals Board. The HHS Department of Appeals Board provides independent review of disputed decisions in a wide range of HHS programs, including administrative review of claims for entitlement to Medicare and individual claims for Medicare coverage and payment filed by beneficiaries or health care providers/suppliers.
  - NTAP applicants should have the right to seek judicial review if dissatisfied with administrative review.
  - The Secretary should be required to review NTAP decisions for FY 2016 and later fiscal years. The current discussion draft focuses on discharges as the triggering event and that does not appear to be appropriate given that this provision pertains to NTAP application denials.
- Section 4201 (b) would replace Healthcare Common Procedure Coding System (HCPCS) codes with National Drug Codes (NDC) for drugs and biologicals billed under Medicare Part B, presumably to shorten the timeframe for issuance of codes for new products. The draft legislation also includes language that addresses payment for Part B covered drugs and biologicals under the proposed NDC coding mechanism.

Concerns: HCPCS codes have long been used to bill physician-administered drugs under the medical benefit, whereas NDCs have been used in retail pharmacy transactions under the pharmacy benefit. There are significance differences between the codes sets, as well as the medical benefit vs. pharmacy benefit claims systems. This proposal to replace HCPCS codes with NDCs has numerous logistical and implementation issues and would be burdensome for providers and payers alike. Key issues include:

- Unclear Billing Amount: Unlike HCPCS codes, NDCs provide no mechanism for billing for doses that are less than the amount represented by the NDC. Providers commonly need to bill for less than the NDC amount and this proposal does not make it possible to appropriately bill for products in multi-dose vials.
- Inability to Identify NDCs: For products that are supplied in multi-packs, providers may not have systems in place that track the NDC once the packs are opened and separated, creating a risk that an incorrect NDC would be reported.
- Inconsistent with HIPAA Transaction Standards: Under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), HHS has



adopted HCPCS codes as the standard code set for billing for physician-administered drugs for all payers, including CMS, state Medicaid agencies, and private payers. This legislative proposal would appear to change the standard code set for Medicare Part B only. The repercussions for other payers are unclear. In addition, HIPAA requires a consensus-building process, including rulemaking, to change standard code sets. This proposal would short circuit the HIPAA requirement to build stakeholder consensus before changing a code set.

- Provider Billing System Limitations: It would be burdensome for virtually all providers to implement as their billing systems would need to be reconfigured from five-digit HCPCS codes to eleven-digit NDCs. Furthermore, providers would be forced to use NDCs for their Medicare claims, but HCPCS for claims submitted to other payers.
- CMS and Private Payer Administrative Concerns: Similarly, it would also be burdensome for CMS to implement and manage as the agency would have to create payment rates for significantly more codes than they currently do and would also need to reconfigure their claims processing systems and forms to accommodate NDCs. There would be an additional burden to keep the Medicare data set current as NDC codes can be changed or newly issued frequently. Private payers would be required by HIPAA to continue to use HCPCS codes, yet CMS would no longer issue or maintain HCPCS codes for drugs and biologicals.
- No Impact on Time to Establish ASP: This proposal would have no impact on speeding the ASP rate-setting process, as CMS would still need sales data, submitted by the manufacturer quarterly, to establish ASP payment rates.
- Statute on Average Sales Price: The proposal opens up the part of the Medicare statute that addresses Part B drug and biological payment (*i.e.*, Average Sales Price or ASP), which is not necessary to address timeliness for issuance of new codes.

Recommendation: A better policy solution to achieve timely issuance of Part B drug and biological billing codes would be to require CMS to issue HCPCS codes on a rolling or quarterly basis after drug and biological products are approved. CMS has a proven track record issuing HCPCS codes quarterly for use in other settings.

#### **Title IV, Subtitle S – Continuing Medical Education Sunshine Exemption**

- Generally support excluding peer-reviewed journals, journal reprints, journal supplements, and medical textbooks from the reporting requirement under the Sunshine Act. However, regarding terminology, the term “continuing medical education” has a specific meaning and refers to those symposia attended by health care providers that may have industry support. The proposed insert of new clause (xiii) (page 344, line 24) seems to have a broader purpose along lines of intending to capture anything that could be used for physician education. Suggest considering revising terminology so as to mitigate the risk of confusion.

## **Title V, Subtitle B – 21<sup>st</sup> Century Manufacturing**

- We are supportive of ensuring a continued dialogue with the FDA on novel manufacturing techniques and new technology. The proposed language in Section 5021 (page 349) is very broad and may benefit from inclusion of specific provisions illustrating the type of concepts which may help speed up the development of new medical products. With this mind, we've attached a document outlining such a proposal which we've shared with you previously.<sup>5</sup>

In addition, it should be noted that a one year requirement for putting out final guidance in this area of novel approaches and technologies is likely not feasible. It may be more beneficial to set up a process for a public meeting and proposed rule in order for the Agency to solicit input and receive detailed feedback from stakeholders. This would help alleviate the sole burden on the Agency to come up with proposals and also ensure stakeholders are able to share with the Agency detailed suggestions around novel ideas and approaches.

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<sup>5</sup> See attachment titled "Amgen 21<sup>st</sup> Century Cures – Early Clinical Development Proposal"

## A BILL

To amend the Federal Food, Drug, and Cosmetic Act to accelerate the development of innovative drugs and biological products and for other purposes.

1       *Be it enacted by the Senate and House of Representatives of the United States of*  
2       *America in Congress assembled,*

3       **SEC. 1. SHORT TITLE.**

4       This Act may be cited as the \_\_\_\_\_.

5       **SEC. 2. STREAMLINING EARLY DEVELOPMENT OF NEW DRUGS AND BIOLOGICAL**  
6       **PRODUCTS.**

7       (a) PUBLIC MEETING.—Within [X] months of the date of enactment, the Secretary  
8       shall hold a public meeting to solicit recommendations on novel approaches to reduce the  
9       regulatory burdens associated with manufacturing process development during preclinical  
10      and early clinical development of new drugs and biological products, while ensuring  
11      compliance with section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (21  
12      U.S.C. 351(a)(2)(B)). In particular, the Secretary shall solicit recommendations on  
13      approaches to—

14               (1) increase regulatory flexibility in the requirements for submission of  
15      chemistry, manufacturing, and controls information under section 505(i)(2)(B) of  
16      the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)(2)(B)) and section  
17      351(a)(3) of the Public Health Service Act (42 U.S.C. 262(a)(3)) during the early  
18      clinical development of new drugs and biological products;

1 (2) better tailor the current good manufacturing practice requirements  
2 applicable to a new drug or biological product to the phase of development of,  
3 and available knowledge about the risks and benefits of, such new drug or  
4 biological product;

5 (3) expand upon the approach described in the Food and Drug  
6 Administration guidance entitled “Guidance for Industry, Investigators, and  
7 Reviewers: Exploratory IND Studies,” dated January 2006, to reduce the  
8 regulatory burden for exploratory proof-of-concept studies in order to better  
9 facilitate exploratory clinical testing of biological products; and

10 (4) utilize computerized systems that model manufacturing steps and other  
11 technological tools in developing the chemistry, manufacturing and controls  
12 information for submission under section 505(i)(2)(B) of the Federal Food, Drug,  
13 and Cosmetic Act (21 U.S.C. 355(i)(2)(B)) and section 351(a)(3) of the Public  
14 Health Service Act (42 U.S.C. 262(a)(3)) and for other regulatory purposes.

15 (b) GUIDANCE.—

16 (1) No later than [X] months after the date of the public meeting under  
17 subsection (a), the Secretary shall publish draft guidance proposing to implement  
18 approaches to reduce the regulatory burdens associated with manufacturing  
19 process development during preclinical and early clinical development of new  
20 drugs and biological products. Such draft guidance shall include  
21 recommendations to further the objectives described in paragraphs (1) through (4)  
22 of subsection (a).

1                   (2) Within [X] after the publication of such draft guidance under  
2                   paragraph (1) and after notice and opportunity for public comment on such draft  
3                   guidance, the Secretary shall publish final guidance on such matters described in  
4                   paragraph (1).

5                   (3) The draft guidance described in paragraph (1) and the final guidance  
6                   described in paragraph (2) shall provide that new drugs and biological products  
7                   that adhere to the recommendations set forth in such guidance will not be deemed  
8                   to be in violation of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic  
9                   Act (21 U.S.C. 351(a)(2)(B)).

10                  (c) DEFINITIONS.— In this section—

11                   (1) The term “drug” has the meaning given to that term in section  
12                   201(g)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(g)(1));  
13                   and

14                   (2) The term “biological product” has the meaning given to it in section  
15                   351(i)(1) of the Public Health Service Act (42 U.S.C. 262(i)(1)).

## A BILL

To amend the Federal Food, Drug, and Cosmetic Act to accelerate the development of innovative medicines and combination products and for other purposes.

1        *Be it enacted by the Senate and House of Representatives of the United States of*  
2        *America in Congress assembled,*

3        **SEC. 1. SHORT TITLE.**

4        This Act may be cited as the \_\_\_\_\_.

5        **SEC. 2. IMPROVING COMBINATION PRODUCT REGULATION.**

6        (a) PERFORMANCE GOALS FOR ALL CENTERS INVOLVED IN REVIEWING  
7        COMBINATION PRODUCTS.—In connection with the reauthorization of the Prescription  
8        Drug User Fee Amendments of 2012 and the Medical Device User Fee Amendments of  
9        2012, the Secretary shall establish performance goals for the premarket review of  
10       combination products that apply to both the review activities of the agency center with  
11       primary jurisdiction and the consulting agency center or centers under section 503(g) of  
12       the Federal Food, Drug and Cosmetic Act (21 U.S.C. 353(g)). The Secretary shall  
13       specify such goals in the letters to the Chairman of the Committee on Health, Education,  
14       Labor, and Pensions of the Senate and the Chairman of the Committee on Energy and  
15       Commerce of the House of Representatives that identify review performance goals for  
16       purposes of parts 2 and 3 of subchapter C of chapter VII of the Federal Food, Drug, and  
17       Cosmetic Act.

18       (b) PROCEDURES AND MILESTONES FOR COMBINATION PRODUCT REVIEWS.—Prior  
19       to the reauthorizations described in subsection (a), the Secretary shall update existing

1 good review management principles and practices of the Food and Drug Administration  
2 to include milestone dates for review activities of the consulting agency center for a  
3 combination product.

4 (c) GUIDANCE TO IMPROVE REGULATION OF COMBINATION PRODUCTS.—Section  
5 503(g) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 353(g)) is amended by  
6 adding at the end the following—

7 “(6) To promote clarity in the regulation of combination products and  
8 expedite their review, within [X] after the date of enactment of this Act, the  
9 Secretary shall publish draft guidance regarding procedures and processes for  
10 premarket review of combination products. Such draft guidance shall establish  
11 procedures and processes that—

12 “(A) ensure appropriate and timely participation by the consulting agency  
13 center or centers in the review activities of the agency center with  
14 primary jurisdiction, by providing that each consulting agency center  
15 should complete its review activities before, or at the same time as, the  
16 agency center with primary jurisdiction;

17 “(B) ensure that the agency center with primary jurisdiction, the consulting  
18 agency center or centers, and the Office described in paragraph (4) of this  
19 subsection provide consistent advice to the sponsor, including by:

20 “(i) providing for attendance of personnel from the consulting agency  
21 center or centers and the Office at meetings between the sponsor  
22 and the agency center with primary jurisdiction;

1                   "(ii) providing that the consulting agency center or centers and the  
2                   Office may respond in writing to sponsor submissions, inquiries, or  
3                   communications regarding the development of combination  
4                   products, and providing that such written responses will identify  
5                   the agency center or Office that authored each response.

6                   "(C) ensure the referral of review issues to the agency center with the greatest  
7                   expertise and experience over the subject matter and enable direct  
8                   communication between the sponsor and the agency center or centers to  
9                   which the review issues are referred; and

10                  "(D) state that the sponsor of a combination product will be provided with a  
11                  written justification for any decisions of the Food and Drug  
12                  Administration to deviate from a guidance document in accordance with  
13                  21 C.F.R. 10.115(d)(3) or from standard agency practice with respect to  
14                  the such combination product.

15                  Within [X] after the publication of such draft guidance and after notice and  
16                  opportunity for public comment on such draft guidance, the Secretary shall  
17                  publish final guidance on such matters described in this paragraph.

18                  (d) NEW DELIVERY MECHANISMS FOR DRUGS.—

19                         (1) PUBLIC MEETING.—Within [X] months after the date of enactment of  
20                         this Act, the Secretary shall hold a public meeting to solicit advice and  
21                         recommendations from a variety of stakeholders on approaches to expedite access  
22                         to new delivery mechanisms for drugs and for multiple drugs using the same  
23                         delivery platform. Any such approach adopted by the Secretary shall ensure that



1 device constituents of combination products are regulated consistent with sections  
2 513(a)(3)(D)(ii)&(iii) and 513(i)(1)(D) of the Federal Food, Drug, and Cosmetic  
3 Act (21 U.S.C. 360c(a)(3)(D)(ii)&(iii), 360c(i)(1)(D)).

4 (2) REPORT.—Within [X] months after the date of the public meeting  
5 under subsection (d)(1), the Secretary shall submit to Congress a report that  
6 includes a strategic plan for expediting access to new delivery mechanisms for  
7 drugs and for multiple drugs using the same delivery platform.

**RETAIN THE CURRENT FDAMA 114 FRAMEWORK AND**  
**CLARIFY KEY STATUTORY TERMS**

Sec. 502 [352] Misbranded Drugs and Devices.<sup>1</sup>

A drug or device shall be deemed to be misbranded—

(a)

- (1) If its labeling is false or misleading in any particular. Health care economic information provided to a payer, formulary committee, or other similar entity, in the course of the payer, committee, or other similar entity carrying out its responsibilities for the selection of drugs for managed care or other similar organizations, shall not be considered to be false or misleading under this paragraph if the health care economic information ~~directly~~ relates to an indication approved under section 505 or under section 351 of the Public Health Service Act for such drug, ~~and~~ is based on competent and reliable scientific evidence, and includes, where applicable, a conspicuous and prominent statement describing any differences between the information and the indication approved under section 505 or under section 351 of the Public Health Service Act. The requirements set forth in section 505(a) or in section 351 of the Public Health Service Act shall not apply to health care economic information provided to such a payer, committee, or entity in accordance with this paragraph. Information that is relevant to the substantiation of the health care economic information presented pursuant to this paragraph shall be made available to the Secretary upon request.
- (2) For purposes of this subsection, In this paragraph, ~~The~~ term “health care economic information” means any analysis (including the data, inputs, clinical or other assumptions, methods, results, and other components comprising the analysis) that identifies, measures, or describes the consequences, including the separate or aggregated clinical consequences and costs of the represented health outcomes, of the use of a drug. Such analyses may be comparative to the use of another drug, to another health care intervention, or to no intervention.

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<sup>1</sup> Proposed deletions are reflected by stricken text, and proposed additions are noted by underlining.



February 13, 2015

### **Apotex Comments on the “21<sup>st</sup> Century Cures Act”**

Apotex appreciates this opportunity to comment on the current discussion draft of the “21<sup>st</sup> Century Cures Act.” Apotex supports the goals behind the 21<sup>st</sup> Century Cures Act and applauds Chairman Upton and Congresswoman DeGette for their leadership and hard work on this critical public health initiative. We look forward to working with the Committee to facilitate the discovery and approval of new cures and enhance the Hatch-Waxman Act’s capacity to spur innovation and increase access to affordable medicines through competitive forces.

#### **Section 1241, “Extended Exclusivity Period for Certain New Drug Application and Abbreviated New Drug Applications”**

This comment only addresses Section 1241 of the discussion draft “Extended Exclusivity Period for Certain New Drug Applications and Abbreviated New Drug Applications.”<sup>1</sup> Section 1241 would enhance the existing 3-year “new clinical studies” exclusivity that can be earned by the sponsor of a new drug application (NDA). The exclusivity is awarded when the approval of an original NDA or supplement to an approved NDA is supported by a new clinical study that is

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<sup>1</sup> Apotex agrees with the comments previously submitted to the Committee by the Generic Pharmaceutical Association and looks forward to working with the Committee on these issues as well.

essential to the approval, and the study was conducted by or for the NDA sponsor. That 3-year exclusivity blocks the final approval of an abbreviated new drug application (ANDA) or 505(b)(2) NDA (where the NDA sponsor does not own or have a right of reference to the entire data package needed to support approval) for 3 years. Section 505(j)(5)(F)(iii) and (iv) and 505(c)(3)(E)(iii) and (iv) of the FDC Act, 21 U.S.C. § 355(j)(5)(F)(iii) and (iv) and § 355(c)(3)(E)(iii) and (iv). Specifically, Section 1241 would establish a procedure under which existing 3-year “new clinical studies” exclusivity could be extended by up to an additional 2 years under certain circumstances. Although Apotex understands and supports the need to ensure that there are sufficient incentives for innovator drug companies to facilitate the discovery of new cures, Apotex has three fundamental concerns with the approach set forth in the discussion draft.

First, from a systemic perspective, solely raising the 3-year new clinical studies exclusivity without addressing deficiencies in the current filing process for these products would disrupt the balance between innovation and competition that Hatch-Waxman relies on to spur the development of new cures while increasing access to affordable medicine through robust competition. A detailed explanation of the deficiencies and an alternative proposal to the current approach of Section 1214 which would correct them follows later in these comments.

Second, and importantly, the approach of the current discussion draft (to add new clause (vi) to Section 505(j)(5)(F) of the FDC Act for extending 3-year “new clinical studies” exclusivity with regard to the approval of ANDAs) would jeopardize the 180-day exclusivity rights earned by sponsors of ANDAs that qualify as “first applicants.” The opportunity to market a generic drug product for 180 days with no – or limited – generic competition is a very valuable incentive for the generic drug industry. Absent a meaningful 180-day exclusivity

period, there could be reduced incentive to engage in product development and costly patent infringement litigation.

Generic manufacturers filing Paragraph IV challenges against reference products eligible for extended 5-year “new clinical studies” exclusivity, as contemplated by the discussion draft, may forfeit their 180-day exclusivity rights if they win patent challenges before the expiry of the 5-year exclusivity period. As explained below, simply lengthening “new clinical studies” exclusivity from 3 to 5 years will thus diminish the value of 180-day exclusivity as ANDA first applicants could find themselves forfeiting earned 180-day exclusivity before having a chance to use it.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) amended the FDC Act to include provisions under which a first applicant’s 180-day exclusivity rights can be forfeited. In relevant part, under the “failure to market” forfeiture condition in Section 505(j)(5)(D)(i)(I) of the FDC Act, 21 U.S.C. § 355(j)(5)(D)(i)(I), a first applicant would forfeit its 180-day exclusivity rights if it has not received final ANDA approval and begun marketing 75 days after the date on which, with respect to each patent for which that first applicant submitted a Paragraph IV certification, there is a final court decision (namely, a Federal Circuit decision, or a district court decision that is not appealed to the Federal Circuit) that the patent is invalid or not infringed.

Under current law, the 3-year “new clinical studies” exclusivity period is very unlikely to lead to forfeiture of 180-day exclusivity under this forfeiture provision, as there is very little likelihood that a first applicant will have obtained a favorable final court decision with regard to

each Paragraph IV patent before the 3-year exclusivity period has expired.<sup>2</sup> If, however, the current 3-year exclusivity period is extended to 5 years (as under the approach of the discussion draft), forfeiture of 180-day exclusivity rights would be much more likely. Specifically, it seems to Apotex that there is a reasonable likelihood that an ANDA could be prepared and submitted to FDA after the approval of a product with extended 5-year “new clinical studies” exclusivity, with all patent infringement litigation concluded in the ANDA sponsor’s favor well before the 5-year “new clinical studies” exclusivity expires. The result would be the forfeiture of the first applicant’s 180-day exclusivity rights because the first applicant would be blocked by the 5-year “new clinical studies” exclusivity from receiving final ANDA approval and entering the market before its exclusivity has been forfeited.

Third, Apotex is also concerned with the discussion draft’s approach of establishing a number of criteria in new clause (vi) of Section 505(j)(5)(F) of the FDC Act for qualifying for the extended 5-year period of exclusivity, which criteria are to be defined by regulation by FDA. The criteria in the discussion draft, such as greater patient adherence, reduced public health risks, reduced side effects, systemic benefits to the health care system, and comparable patient benefits, will be open to interpretation. This will saddle FDA with a difficult task. Both innovator and generic drug sponsors that are disadvantaged by FDA decision-making are likely to resort to litigation against the Agency. Indeed, there is a long history of litigation resulting from industry

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<sup>2</sup> The “failure to market” forfeiture condition includes a complex set of interrelated “earlier of” and “later of” dates. As a practical matter, the two dates in Section 505(j)(5)(D)(i)(I)(aa) (namely, the earlier of 75 days after the date of the final approval of the first applicant’s ANDA or 30 months after the date of submission of the first applicant’s ANDA) are unlikely to be controlling because the (aa) date will be no later than 30 months after the date of submission of the first applicant’s ANDA. It is highly unlikely that there will be final decisions in all patent litigation in a first applicant’s favor within that time period. Thus, the dates in (bb) are likely to be controlling, as they are likely to be later than the (aa) date. In particular, the dates in Section 505(j)(5)(D)(i)(I)(bb)(AA), with regard to final court decisions that the patents are invalid or not infringed, are likely to be controlling and could lead to forfeiture of 180-day exclusivity.

disagreement with FDA exclusivity determinations. Such litigation will divert scarce FDA resources that could be better spent fulfilling FDA’s public health mission.

On a related note, Section 1241(c) of the discussion draft would require FDA to publish final implementing regulations within 180 days after the date of enactment. In Apotex’s view, that is not a realistic timeframe for FDA to issue final regulations (or even proposed regulations or guidance). Apotex’s concern about the rulemaking timeline of the discussion draft is supported by FDA’s track record. For example, the Drug Price Competition and Patent Term Restoration Act of 1984, commonly called Hatch-Waxman, added the current ANDA and related provisions to the FDC Act. Hatch-Waxman required FDA to issue regulations within one year of its date of enactment (namely, by September 24, 1985). Pub. L. No. 98-417, Section 105(a) (98 Stat. 1585, 1597). Despite the statutory deadline, FDA did not issue a proposed rule until 1989 (54 Fed. Reg. 28,872; Jul. 10, 1989). FDA issued its final rule in two parts in 1992 (57 Fed. Reg. 17,950; Apr. 28, 1992) and 1994 (59 Fed. Reg. 50,338; Oct. 3, 1994)). Thus, FDA was more than nine years late in fulfilling its statutory rulemaking obligation. Earlier this month, FDA issued a proposed rule to implement part of the MMA amendments to the FDC Act (80 Fed. Reg. 6802; Feb. 6, 2015). That proposed rule – issued over 11 years after the MMA’s enactment – only addresses provision of notice of a Paragraph IV certification and the availability of 30-month litigation stays; it does not address the more difficult and more contentious 180-day exclusivity changes made by the MMA. Simply stated, we do not think there is any realistic likelihood that FDA could meet the rulemaking timeline set forth in the discussion draft. The inevitable lack of timely regulations (or guidance) regarding how FDA intends to interpret the provisions related to the extension of 3-year “new clinical studies” exclusivity could thus create significant uncertainty for industry and other stakeholders.

### **Alternative to Section 1241 Language**

Despite our concerns with the discussion draft’s approach, Apotex agrees with the notion that revision of the 3-year “new clinical studies” exclusivity provisions of the FDC Act is necessary. In order to facilitate the submission of high quality ANDAs that do not force the Agency to expend scarce resources on applications that were hastily prepared in a rush to secure 180 day exclusivity rights – and thus exacerbate the backlog problem by prolonging the approval of high quality applications waiting for FDA review – Apotex believes that the 3-year exclusivity provisions should be revised to mimic the operation of the current 5-year “new chemical entity” (NCE) exclusivity provisions for NDA sponsors, where the NDA approval is the first approval for the drug product’s active ingredient. Section 505(j)(5)(F)(ii) (with regard to ANDAs) and 505(c)(3)(E)(ii) (with regard to 505(b)(2) NDAs) of the FDC Act, 21 U.S.C. § 355(j)(5)(F)(ii) and § 355(c)(3)(E)(ii).

While the impetus for implementing such a change is to facilitate the submission of high quality ANDAs and thus bring efficiencies to the generic drug approval process that will benefit all stakeholders, such a system would also have the practical effect of increasing new clinical studies exclusivity to 5.5 years, consistent with the intent of Section 1241 as currently drafted, but without all the attendant problems. Apotex would support such an outcome given the efficiencies that a revamped 3-year new clinical studies filing process would bring to the ANDA and 505(b)(2) approval process. Such an outcome would appropriately maintain the critical balance between competition and innovation that lies at the heart of Hatch-Waxman’s historic success.



### **Details of the 3-Year Filing Process Deficiency and Proposed Solution**

One substantial area of concern for which FDA has chided the generic drug industry over the years is the submission of low-quality ANDAs that were hastily crafted in a rush to qualify for 180-day exclusivity. The submission of low-quality applications consumes scarce FDA resources, contributing to longer approval times and the exacerbation of the ANDA review and approval backlog. Companies developing high-quality ANDAs, and the public, are effectively penalized as a result.

The submission of low-quality applications to FDA is of particular concern where the innovator product is protected by 3-year “new clinical studies” exclusivity. For these products, the only timing limitation is that FDA cannot approve an ANDA until 3 years after the approval of the reference drug product. Because there is no restriction on when an ANDA can be submitted to FDA, some companies have found it beneficial to “cut corners” and quickly develop and submit marginal ANDAs in an attempt to qualify for 180-day exclusivity.

Moreover, there have been questionable instances in which generic firms have submitted ANDAs within days or weeks after the reference listed drug product was first approved and reached the market. The only logical conclusion is that the proposed generic product was developed and tested *before* the reference product was available. Such practices could well result in the applicants not understanding the reference listed product and submitting poor quality applications. FDA must then spend its resources reviewing applications for which the sponsors may not have evaluated the Quality Target Product Profile (QTPP) of the reference listed drug

before developing its generic version. This, in turn, delays the approval of high-quality applications.

To promote the submission of high-quality ANDAs, the 3-year “new clinical studies” exclusivity provisions of Hatch-Waxman should be amended to make them parallel with 5-year NCE exclusivity. An ANDA for a copy of a reference product protected by 5-year NCE exclusivity cannot be submitted to FDA until 5 years after the approval of the innovator product, except that a Paragraph IV ANDA can be submitted after 4 years. Applying that approach to 3-year “new clinical studies” exclusivity, no ANDA could be submitted to FDA until 3 years after approval of an innovator product protected by 3-year “new clinical studies” exclusivity, except that a Paragraph IV ANDA could be submitted 2 years after the approval of the innovator product being copied.

This approach would promote the submission of high-quality ANDAs and speed approval times while ensuring that sponsors are still afforded sufficient opportunity to qualify for 180-day exclusivity, benefiting the Agency, industry, and the public alike. Revising 3-year “new clinical studies” exclusivity as contemplated by Apotex would achieve the discussion draft’s objective of providing, as a practical matter, a longer exclusivity period to incentivize the development of new cures. At the same time, it would avoid jeopardizing the first applicant’s 180-day exclusivity and avoid a new era of litigation over criteria that could prove difficult to clearly define and implement consistently. It would represent a balanced approach to ensure FDA resources to approve ANDAs are used in the most efficient manner possible as the Agency works on the significant challenge of eliminating the ANDA backlog.

Apotex is in the process of preparing and vetting draft legislative language and accompanying materials on our proposed “fix” to 3-year “new clinical studies” exclusivity. Apotex looks forward to sharing these materials with the Committee in the very near future.

\* \* \*

Apotex is one of the world’s leading generic pharmaceutical manufacturers, employing approximately 10,000 people across the globe. The company’s U.S. headquarters, Apotex Corp., is based in Weston, Florida. With its worldwide manufacturing sites, Apotex can produce up to 24 billion dosages per year. It produces 300 medicines in 4,000 dosages and formats that are exported to 115 countries. It has 500 products under development and will spend \$2 billion over the next 10 years on research and development.

Apotex appreciates this opportunity to submit comments on Section 1241 of the discussion draft. Apotex may submit separate comments on other provisions of the draft.

February 13, 2015

The Honorable Fred Upton  
2183 Rayburn House Office Building  
Washington, DC 20515

Dear Chairman Upton:

The Arthritis Foundation, on behalf of the more than 50 million adults and children in the U.S. living with arthritis, welcomes the opportunity to comment on the draft 21<sup>st</sup> Century Cures legislation. There are over 100 types of arthritis, and there is no cure for the disease. Further, certain types of arthritis like osteoarthritis – which affects over 27 million Americans – don't have any effective pharmaceutical treatments. For others, treatment can be very complex - people with auto-immune forms of arthritis like rheumatoid arthritis often rely on multiple types of drugs, including biologic drugs, to manage their disease.

Reducing regulatory and other barriers to research that can accelerate discovery, development, and delivery of medical treatments can greatly benefit people with arthritis. Your legislation goes a long way towards addressing research needs around discovery and development of treatments. However, we would like to see more emphasis on the delivery pillar. The costs of drugs are prohibitive for many people with arthritis, even with insurance. Insurance designs like specialty tiers require people to pay up to 50% of the cost of their drugs out-of-pocket. For people who rely on biologic drugs – like those to treat rheumatoid arthritis – this can represent thousands of dollars each month.

The Arthritis Foundation would like to offer the following comments on your draft legislation.

Title I – Putting Patients First by Incorporating their Perspectives into the Regulatory Process and Addressing Unmet Medical Needs

Subtitle A – Patient Focused Drug Development

The Arthritis Foundation believes that patient perspectives during the drug development process are vital to developing drugs that will best suit the needs of patients. Many people with arthritis are on multiple medications, and for complex forms of the disease, it is not uncommon for patients to take 40 or more pills a day. It is important that the FDA understands the patient experience, including what types of reactions and side effects they have to medications, and the level of difficulty in accessing and adhering to medications. The Arthritis Foundation made several suggestions to the FDA in their recent request for comments on patient perspectives in the drug development process, including the creation of a patient portal on the FDA website, the use of tele-town halls, webinars, and forums to educate patients about drug development, inclusion of arthritis in the disease-specific meetings calendar, and more robust use of patient registries to collect data on patient experiences.

We support your effort to strengthen the patient perspective in FDA's regulatory processes, and agree that a more structured framework for incorporating patients will help ensure their needs are addressed at every step of the process. However, we also urge you to identify ways patients can be involved early in the drug development process, and we seek clarification on how drug sponsors may be able to communicate with patients on drugs they are working on without legal ramifications.

## Subtitle B – Surrogate Endpoint Qualification and Utilization

Strengthening the surrogate endpoint qualification process and identification of biomarkers is vitally important to people with arthritis. This is relevant to most, if not all types of arthritis. For example, although osteoarthritis affects 27 million Americans, there is no qualified biomarker for the disease, and no effective pharmaceutical treatment.

We support the effort to make it easier to qualify endpoints, which can help bring drugs for osteoarthritis to market. However, we urge you to authorize additional funds in this provision to give the FDA the resources to implement this provision.

## Subtitle C and F – Approval of Breakthrough Therapies and Devices

Access to breakthrough therapies and devices is important to people with arthritis, particularly persons with rare and/or terminal types of arthritis. The Arthritis Foundation is pleased you are addressing ways to bring breakthrough therapies to patients more quickly, but we seek clarification on the definition for unmet medical need, in addition to how rigorous patient safety standards will be kept in place when considering early stage clinical data.

## Subtitle G – Expanded Access

Expanded access programs can help patients to access drugs they would not otherwise have access to. Currently, even if a patient meets the criteria for compassionate use programs, there may still be obstacles, including:

- The physician must determine that the probable risk from the drug is not greater than the probable risk from the disease;
- The company that makes the drug is not required to offer it outside their clinical trials, and they may not be willing or able to do so;
- The company may not have enough of the drug available for all patients requesting expanded access. Some companies establish a lottery system to determine which patients will have treatment access, and others make the decision on a case-by-case basis;
- Investigational drugs are expensive to make. Most insurance companies will not pay for access to an investigational drug and there may be additional cost for administering and monitoring them.

## Subtitle H – Facilitating Responsible Communication of Scientific and Medical Developments

Many patients rely on off-label drugs to treat their disease. For example, low doses of certain antidepressants, muscle relaxants, and anti-seizure medications can all help relieve symptoms of fibromyalgia. The Arthritis Foundation believes preservation of the physician-patient relationship is a vital part of patient care. Physicians should be able to prescribe the drugs that will best treat their patients without fear of violating regulatory policies.

## Subtitle K – Cures Acceleration Network

The Cures Acceleration Network holds great promise for getting treatments to patients more quickly. We support your effort to strengthen CAN by giving it more flexibility. We particularly support the provision authorizing additional funds for research on repurposing drugs. Many drugs used to treat arthritis were developed for other diseases like cancer. For example, methotrexate is a form of chemotherapy that many people with auto-immune forms of arthritis use to help manage their symptoms. Our hope is that drugs currently in the pipeline for other auto-immune and inflammatory diseases and cancer will also be relevant to arthritis prevention and treatment.

## Subtitle L – Dormant Therapies

Many drugs for arthritis, including those for osteoarthritis, have been abandoned because of their failure to meet a clinical endpoint. We are concerned that over time, manufacturers may choose not to re-investigate the drug because the patent has expired or will expire before the research is completed and the time it takes to go through the federal approval process. This provision could help incentivize manufacturers to re-investigate dormant therapies for arthritis. However, we would seek clarification on the definition of unmet medical need and the process by which this provision will be implemented.

## Subtitle M – New Therapeutic Entities

As stated above, many drugs for arthritis, like those for osteoarthritis, fail to meet clinical endpoints. Investigators do not fully understand the pathophysiology of the disease, and therefore do not have the correct patients enrolled in clinical trials and thus cannot demonstrate success. Extending exclusivity for two years could incentivize more research into arthritis drugs and greatly benefit patients waiting for effective treatments for their disease.

## Subtitle N – Orphan Product Extensions Now

There are several types of arthritis among both children and adults that are considered rare and have orphan drugs. For example, myositis is an inflammatory disease that affects the muscles, and can cause flares, muscle weakness, lung and breathing problems, systemic symptoms like fever and weight loss, and joint pain. There are only 50,000-75,000 people in the country with the disease in the US; there is no cure and for some forms of the disease, there is no effective treatment. Providing additional exclusivity for a drug that treats a rare disease can benefit people who suffer from rare forms of arthritis.

## Title II – Building the Foundation for 21<sup>st</sup> Century Medicine, Including Helping Young Scientists

### Subtitle A – 21<sup>st</sup> Century Cures Consortium Act

Public-private partnerships have great potential for accelerating the discovery and development of drugs, and increasing collaboration and innovation across sectors of the research enterprise. We support your effort to increase the level of public-private partnerships through a consortium based on the European Union's Innovation Medicines Initiative.

### Subtitle B – Medical Product Innovation Advisory Committee

It is important for Congress to be continually advised by the scientific community on the discovery-development-delivery cycle. We urge you to include a patient representative on this panel, as the patient perspective is an important component of the research enterprise, particularly as it relates to the delivery of new drugs.

### Subtitle F – Building a 21<sup>st</sup> Century Cures Data Sharing Framework

Data sharing is an important component to improving biomedical research. Patients and physicians need better ways of becoming informed of clinical trials, and researchers need access to data that will help direct them towards the most pressing research needs and ultimately improving quality of care. A data sharing framework could help achieve this goal. In terms of using registries, we recommend you include patient advocacy groups in the consultation with clinical experts section, as organizations like the Arthritis Foundation are heavily involved in registries.

### Subtitle G – Utilizing Real-World Evidence

Utilizing data on how drugs affect patients and how patients experience symptoms is critical to advancing research. This provision fits in line with the Arthritis Foundation's Scientific Strategy, supporting data collection from registries, and other federal efforts like PCORI's PCORNET.

#### Subtitle H – Coverage with Evidence Development

Out-of-pocket costs are a huge concern for many people with arthritis. The Arthritis Foundation supports the effort to give Medicare beneficiaries more coverage with regard to drugs from clinical trials in which they participate. This provision should include a process to help CMS develop a better coverage decision process.

#### Subtitle J – Combination Products

There is a number of combination products used to administer arthritis treatments. As you continue your work on regulatory guidance for combination products, the Arthritis Foundation believes that consistency and appropriateness of post-market regulation of combination products is needed, in order to preserve patient safeguards.

#### Subtitle L – NIH-Federal Data Sharing

The Arthritis Foundation believes that data-sharing can help everyone in the research community to better understand and by extension support discovery and development of treatments for disease. Having access to NIH data would help private foundations like the Arthritis Foundation that support research best direct their resources to find a cure.

#### Subtitle M – Accessing, Sharing, and Using Health Data for Research Purposes

Using health data can benefit patients by better informing research needs and improving outcomes. Specific benefits include:

- Guiding immediate action for cases of public health importance;
- Measuring the burden of a disease (or other health-related event), including changes in related factors, the identification of populations at high risk, and the identification of new or emerging health concerns;
- Monitoring trends in the burden of a disease (or other health-related event);
- Guiding the planning, implementation, and evaluation of programs to prevent and control disease, injury, or adverse exposure;
- Evaluating public policy;
- Detecting changes in health practices and the effects of these changes;
- Prioritizing the allocation of health resources;
- Describing the clinical course of disease; and
- Providing a basis for epidemiologic research.

#### Subtitle N – 21<sup>st</sup> Century Chronic Disease Initiative Act

People with arthritis often live with their disease for years and even decades. In addition, more than half of people with other chronic diseases like diabetes (52%), and heart disease (57%) also have arthritis. For people with juvenile arthritis who are on methotrexate and/or biologics, there is a lot of information that is unknown about the long-term impacts of those drugs. A longitudinal study measuring the long-term impact of disease and treatment can help answer many questions about the effects of disease on quality of life and of treatments on long-term health outcomes.

#### Subtitle O – Helping Young Emerging Scientists

Fostering the next generation of researchers is critical to maintaining America's status as a leader in biomedical research. This provision fits in line with the Arthritis Foundation's Scientific Strategy to cultivate young and future scientists in pursuing careers in research. We urge you to provide additional funding to NIH to fund more emerging scientists.

#### Subtitle P – Fostering High-Risk, High-Reward Science

High-risk, high-reward science can yield major breakthroughs, yet the current federal research structure often does not incentivize this type of research. The Arthritis Foundation supports efforts like the Accelerating Medicines Partnership which emphasizes high-risk, high-reward research, and we support efforts to increase this type of research.

#### Subtitle A – Clinical Research Modernization Act

The current IRB process is often cumbersome and can act as a barrier to accelerating research. The Arthritis Foundation supports your effort to streamline this process.

Any changes to the IRB process and the effects on human research protections must stay true to and reaffirm the highest values of protecting the integrity of research, the well-being of human subjects who participate in research, and the trust of the public.

#### Title IV – Accelerating the Discovery, Development, and Delivery Cycle and Continuing 21<sup>st</sup> Century Innovation at NIH, FDA, CDC, and CMS

#### Subtitle H – Local and National Coverage Decision Reforms

The ability of patients to access and afford their treatments is a vital component of the research cycle. Medicare local coverage determination processes are often cumbersome and difficult to navigate. Reforming this system to make it more reliable and effective could greatly improve the ability of beneficiaries to access new treatments in a timely manner. Opportunities for public comment and disclosure of information about determinations will also benefit beneficiaries.

#### Subtitle I – Telemedicine

We appreciate your efforts to address telemedicine. Reducing or containing the cost of healthcare is one of the most important reasons for funding and adopting tele-health technologies. Telemedicine has been shown to reduce the cost of healthcare and increase efficiency through better management of chronic diseases, shared health professional staffing, reduced travel times, and fewer or shorter hospital stays.

Studies have consistently shown that the quality of healthcare services delivered via telemedicine is as good those given in traditional in-person consultations. In some specialties, particularly in mental health and ICU care, telemedicine delivers a superior product, with greater outcomes and patient satisfaction.

There is a dramatic shortage in pediatric rheumatologists, as many states have only 1 pediatric rheumatologist, and several states have none. We encourage you to continue to find pathways to navigate state licensure issues, so that physicians in one state can provide tele-health services to patients in other states, which would greatly benefit our JA population. We urge you to find ways to expand tele-health policies beyond Medicare, so that more patients – like our JA patients – can better access the benefits of telemedicine. We also seek clarification on the budget neutrality requirement, and any unintended consequences or other effects it might have on the Medicare program and patient access to care.

#### Subtitle K – Lowering Medicare Patients OOP Costs

As stated previously, out-of-pocket costs are a huge barrier to many people with arthritis, in terms of accessing and adhering to their medications. We support the goal of this provision in giving beneficiaries more control to choose services that best suit their financial needs. However, we urge you to expand the required list to include information on specialty tier trends and other utilization management tools, and to develop cost-sharing reduction programs as part of this effort.



Out-of-pocket cost issues exist outside the Medicare population as well, and we urge you to expand on this provision for people in the commercial insurance market as well. Including the Patients' Access to Treatment Act, limiting specialty tier cost-sharing, has the potential to dramatically benefit people who currently pay hundreds and even thousands of dollars out-of-pocket every month for drugs that are on specialty tiers.

#### Subtitle S – Continuing Medical Education Sunshine Exemption

The current Sunshine rules have created myriad unintended consequences, such as preventing physicians from being able to participate in certain patient advocacy efforts, and hindering physicians from participating in clinical trials, resulting in many fewer referrals of patients for clinical trials. We support efforts to address some of these unintended consequences, and encourage the Committee to further investigate the possible need of further exemptions from the Sunshine rules.

#### Subtitle D – Medical Device Reforms

Early discussions about comparative effectiveness research (CER) in the United States focused on defining “comparative” and determining the implications for research. Today, the focus has shifted from looking simply at what should be compared to how comparative studies should be designed to answer the practical questions about “effectiveness,” particularly in real world settings. The question now becomes does a treatment, service, or method of delivering care work when applied in real world, clinical practice environments?

To answer that question, health care stakeholders need to think beyond traditional randomized controlled trials (RCTs). One way to consider this is to make use of real-world databases that record the processes of care patients receive, such as electronic medical record (EMR) and medical claims databases. We also might work with patient registries that focus on patients with a specific disease or who receive a particular treatment or device and record the medical outcome for those patients; or these registries could be based on a specific population so that researchers can see what happens within that population.

Again, thank you for the opportunity to comment on the draft 21<sup>st</sup> Century Cures legislation. We look forward to future opportunities to work with you on this legislation. Should you have any questions or if we can be of assistance in any way, please contact Sandie Preiss, Vice President of Advocacy and Access, at 202-887-2910 or [spreiss@arthritis.org](mailto:spreiss@arthritis.org).

Sincerely,

A black rectangular box redacting the signature of Sandie Preiss.

Sandie Preiss  
Vice President, Advocacy and Access  
Arthritis Foundation



**ASSOCIATION FOR MOLECULAR PATHOLOGY**

*Education. Innovation & Improved Patient Care. Advocacy.*

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February 10, 2015

The Honorable Fred Upton  
Chairman  
House Energy and Commerce Committee  
2125 Rayburn House Office Building  
Washington, DC 20515

The Honorable Diana DeGette  
Member  
House Energy and Commerce Committee  
2125 Rayburn House Office Building  
Washington, DC 20515

Sent via e-mail: [Cures@mail.house.gov](mailto:Cures@mail.house.gov)

Re: Regarding the 21st Century Cures Act discussion draft

Dear Members of the Energy and Commerce Committee:

Thank you for the opportunity to submit feedback on the 21<sup>st</sup> Century Cures Act discussion. The Association for Molecular Pathology (AMP) is an international medical and professional association representing approximately 2,300 physicians, doctoral scientists, and medical technologists who perform or are involved with laboratory testing based on knowledge derived from molecular biology, genetics and genomics. Membership includes professionals from the government, academic medicine, clinical testing laboratories, and the in vitro diagnostics (IVD) industry.

AMP applauds the Energy and Commerce Committee on the 21<sup>st</sup> Century Cures Initiative and their efforts to take a holistic look at processes through which new cures are developed, and the positive and negative impacts of regulatory policy. In addition to these comments, AMP submitted comments in June in response to the "21<sup>st</sup> Century Cures: A Call to Action", testimony to the hearing on the topic last September, and last month in response to "A Modernized Framework for Innovative Diagnostic Tests". Links to these documents can be found below.

The 21<sup>st</sup> Century Cures Act addresses many issues and policies and we are greatly appreciative of the effort of Chairman Upton, Representative DeGette, and the many Representatives that have contributed to this overarching proposed legislation that is intended to accelerate the discovery, development, and delivery of preventive measures, treatments, and cures. Below please find our initial response to three sections that are of particular interest to our members. We look forward to having a continued active role in developing the sections related to the regulation of laboratory developed testing services and the National Institutes of Health (NIH) travel policy when the Committee releases updated legislative language.

**Title IV, Subtitle H, Sec. 4161 Improvements in the Medicare Local Coverage Determination (LCD) Process**

AMP appreciates the committee's interest in improving the Medicare Local Coverage Determination (LCD) process and agrees with the proposals outlined in this draft legislation. Any changes made to this process must preserve and improve the public's ability to review and comment on these proposed coverage changes. It is just as important that the Medicare Administrative Contractors (MAC) drafting and finalizing these proposals thoughtfully review the public's input to ensure that patients have access to lifesaving diagnostics.

We strongly support the proposal to require at least 45 days for comment on a new or significantly revised LCD and 60 days for LCDs that propose to limit or preclude coverage for an item or service. These requirements will preserve the public's ability to provide input into these proposals, some of which are very complicated in terms of the science and policies involved. Currently, MACs provide comment periods that may be as short as two weeks, making it nearly impossible to provide thoughtful comments. For draft LCDs related to molecular pathology, a thorough review of the literature must be completed before comments can be drafted, making a standard review period of either 45 or 60 days vital for those who wish to comment.

The Association appreciates the committee's proposal to convene an open, public meeting to review the proposed LCD and receive comments from attendees and for MACs to meet upon request with interested stakeholders within the jurisdiction. MACs should also be required to meet with and consider comments from representatives of interested specialty societies. Specialty societies play an integral role responding to draft LCDs by conducting the reviews of the scientific literature that are necessary to provide meaningful comments. Currently, MACs can ignore their comments because they are only required to respond to those who do business in their jurisdiction. We believe that both groups provide critical input to the MACs on their draft policies. AMP would also like to recommend that MACs be mandated to hold webinars on a regular basis to answer questions and provide clarification on draft LCDs. By utilizing the technology available, many more interested stakeholders will be able to participate in the process than may be able to attend a public meeting.

AMP agrees with the committee's inclusion of language requiring MACs to respond to comments with the release of the final LCD the way federal agencies respond to comments upon the publication of final rules, ensuring that all comments are given the thoughtful review they deserve. Palmetto recently published a final LCD on January 1 for which the comment period closed on December 25. This final LCD does not respond to comments. Given the timing of the final LCD's publication and lack of formal response, it is easy to see why AMP and other commenters may be skeptical that our comments were given the consideration they deserve.

We also strongly support the draft legislation's requirement that MACs wishing to adopt another jurisdiction's LCD undertake the full draft LCD process. However, we believe that the other enhancements to this process are necessary to ensure that the second jurisdiction completes a meaningful review. Noridian has proposed and adopted many of the Palmetto's LCDs in the MoDx program, usually without modification. While Noridian provides for a comment period, it appears evident that they generally intend to ultimately adopt the Palmetto policy. A genuine public comment process is even more critical since those in the subsequent jurisdiction (in this case Noridian) cannot participate in the comment process of the first jurisdiction (in this case Palmetto) and typically do not even know about the LCD in the first jurisdiction, exacerbating the sense that what Palmetto does is already a "done deal" in other jurisdictions. Requiring all jurisdictions to hold public meetings, meet with stakeholders within the jurisdiction, potentially hold a webinar, and then respond to comments will help ensure that the comment period is truly meaningful where the public's comments are thoughtfully considered.

Also, we further recommend that the 21<sup>st</sup> Century Cures Act instructs the Centers for Medicare and Medicaid Services (CMS) to establish a listserv or web-portal where new draft LCDs would be published. AMP is familiar with the current searchable database; however, it is very difficult to navigate. A listserv or web-portal would ensure that those interested would be notified of new drafts upon publication.

#### ***Further Comments on the Palmetto MoDx Pilot***

AMP has been actively engaged in the LCD process, particularly since the launch of Palmetto's MoDx pilot. The *Protecting Access to Medicare Act of 2014* (PAMA) passed by Congress made changes to the LCD process that AMP supported. However, those changes and the changes proposed in this draft legislation do not address all of the issues our members are experiencing as a result of the MoDx pilot. Its lack of transparency, granularity of coverage decisions, and inappropriate evidentiary requirements have been highly problematic – limiting access

to laboratory tests that are often the standard of care – and should not serve as a model for future coverage decisions – molecular or otherwise.

*Greater Coordination among MACs:* PAMA § 216 mandated that CMS consolidate to between one and four MACs nationwide. AMP has repeatedly recommended that no fewer than four MACs, if not more, should be maintained for the review of clinical diagnostic laboratory tests. Having multiple MACs will best allow for the discovery and adoption of good practices with effective regional input. If CMS were to elect to have only a single MAC, then the national coverage determination (NCD) process should be followed as any such decision would in actuality be national in scope. The NCD process would involve more highly structured processes for solicitation of input and transparency of consideration than with local determinations. We recommend that Congress urge CMS to maintain at least four, if not more, MACs.

*Granularity:* CMS has stated that part of the rationale for updating the LCD process for clinical laboratory tests is to bring greater efficiency in the process given that if CMS “require[s] that MACs follow all steps in the current LCD process, we fear that LCDs will not be able to be finalized quickly enough for even a fraction of the thousands of new clinical diagnostic (particularly molecular) tests developed each year.” CMS also asserts that given “multiple molecular diagnostic tests designated to diagnose the same disease may rely on different underlying technologies and therefore, have significantly different performance characteristics,” that Medicare has an “obligation to consider the evidence at a granular level...”

AMP vigorously disputes this underlying rationale. First, there is no meaningful sense in which the statement that there are “thousands of new clinical diagnostic (particularly molecular) tests are developed each year.” This would be like saying that there is no way to develop LCDs that address E&M services because there are hundreds of thousands of practitioners providing them, each in his or her own fashion; indeed, the ability provided by proficiency testing and alternative methods to validate the accuracy and comparability of laboratory tests exceeds that of any other area in clinical medicine. There is no reason tests should be considered for coverage at a more granular level than by CPT code with its associated gene identifiers. If CMS and its MACs consider tests by category for each analyte, as is consistent with the remit of the LCD process of assuring alignment of the service with its medical indications, the volume of tests to be reviewed would be entirely manageable. The standards developed under the *Clinical Laboratory Improvement Amendments*, and not the coverage process, is the best method for addressing the performance characteristics of a given test.

Given the precision of the molecular CPT codes, neither LCD nor NCDs need to be specified beyond the level of the CPT code. The CPT molecular pathology Tier 1, Tier 2 codes with the CPT gene identifiers, and CPT Multianalyte Assays with Algorithmic Analyses (MAAA) codes already cover many of the new tests in current clinical use. These CPT code and CPT gene identifier lists are updated throughout the calendar year and continue to accommodate an expanding list of new tests offered for clinical use that demonstrate a need for new codes. In addition to the resources that are already available in CPT, an official set of gene abbreviation/identifiers have been created for use in the narrative field of the claims form for Tier 2 Molecular Pathology test codes 81400-81408. These CPT molecular pathology code gene identifiers are to give providers, payers, and coders exactly the clinically-relevant level of granularity to facilitate adjudication of claims for all stakeholders. This should provide the granularity that CMS and other payers quite reasonably seek in making molecular coverage decisions. The list was published online on March 12, 2014.

*Evidentiary Standards for Coverage:* Palmetto has issued guidance on the MolDx coverage process entitled, “TheMolDx Clinical Test Evaluation Process (CTEP),” which provides greater clarity about their process but imposes an evidentiary standard that very few laboratories can meet. This high bar –based on standards for new prescription drugs– is *inappropriate* for laboratory tests, which serve a different function and have a widely divergent economic model, which would impede access to most molecular tests. Further, a double-blinded randomized control trial is not the gold standard for diagnostics as it is for therapeutics, because both

characterizing sufficiently similar patient groups and ensuring sufficiently comparable patient management in a diagnostic (as opposed to a therapeutic) setting is not (and has never been) feasible. Drug trials are generally made against a particular standard of care (placebo or alternate drug), but the clinical utility of outcomes for diagnostics can range over many approaches to a patient's illness.<sup>1</sup> Additionally, as an article by the Cochrane collaborative notes, "... direct measurements of whether a particular diagnostic test does in fact enhance patient health are currently very rare," and suggests an alternate paradigm for assessments of clinical laboratory tests.<sup>2</sup>

We vigorously oppose any plans to allow or expand adoption of any such CTEP process for the reasons above, for which there was no opportunity to provide comment to Palmetto, as Palmetto issued CTEP without an opportunity for stakeholder input or comment. We urge the committee to mandate that CMS abandon CTEP and not permit the expansion of the MoDx program as currently configured and conducted.

*FDA Draft Guidance:* This situation is further complicated by the Food and Drug Administration (FDA) draft guidance document to establish a framework of oversight for laboratory developed tests (LDT). Unlike conventional, manufactured, and distributed IVD test kits, LDTs are a medical service throughout the design, performance, and interpretation of the results. As professional services, there are additional opportunities to promote patient safety due to the professional judgment used at every stage. To clearly distinguish the professional services that molecular pathology professionals provide using their education and experience, AMP refers to these services as laboratory developed procedures (LDPs). AMP defines an LDP as "a professional service that encompasses and integrates the design, development, validation, verification, and quality systems used in laboratory testing and interpretative reporting in the context of clinical care."<sup>3</sup> The term LDP better represents the nature of complex laboratory testing, which is very much a medical service, and emphasizes the ongoing involvement of appropriately trained and qualified professionals in every aspect of the procedure, in addition to the provided interpretation. The term also acknowledges the inherent connectedness and interdependence amongst the components of the test, the results, and the role of health care professionals. For these reasons, AMP encourages the Committee to refer to these services as LDPs.

AMP is greatly concerned that FDA's proposed risk-based framework for regulating LDPs will severely disrupt physician and patient access to these vital laboratory services. AMP provided extensive comments to the docket on the guidance that will be of assistance to the Committee as you consider legislative language on this policy area and you may access the comments below. Given the significant impact and potential disruption this proposed framework could have on laboratory services and patient care, AMP has requested that FDA adhere to the Administrative Procedures Act and withdraw the draft guidance and instead pursue notice and comment rulemaking. This would help to ensure transparency in the process, that the FDA provides full consideration of the comments received, and that an economic impact study is conducted prior to finalizing any new regulation.

Earlier this year, AMP published a white paper on *A Molecular Diagnostic Perfect Storm: The Convergence of Regulatory & Reimbursement Forces that Threaten Patient Access to Innovations in Genomic Medicine*. The confluence of the effects of both potential FDA regulation and the MoDx program will only further exacerbate health care access issues. Not only does the MoDx program fail to respect the legitimate concern to avoid disruption of beneficiary access to medically necessary services, but combined with the inability to complete the burdensome and resource intensive medical device pathway, laboratories may have no other choice than to drop clinically necessary tests from their menu. The consequences of this would not only be

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<sup>1</sup> Personalized Medicine Coalition, "*The Future of Coverage and Payment for Personalized Medicine Diagnostics*," 2014. Downloaded from [http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc\\_the\\_future\\_coverage\\_payment\\_personalized\\_medicine\\_diagnostics.pdf](http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/pmc_the_future_coverage_payment_personalized_medicine_diagnostics.pdf)

<sup>2</sup> L. Di Ruffano et al, "How do tests impact on patient health? Development of an Explanatory Framework," Cochrane Methods. Cochrane DB Syst Rev 2011 Suppl 1: 1–40

<sup>3</sup> Ferreira-Gonzalez et al. (2014). Revisiting Oversight and Regulation of Molecular-Based Laboratory-Developed Tests. *The Journal of Molecular Diagnostics*: 16, 3-6.

felt throughout the healthcare system, but there will be a significant disruption to innovation and investment into developing new or modifying existing tests. Expanding the flawed MolDx program beyond Palmetto and finalizing the draft guidance on LDTs would be a mistake and detrimental to patient care and as such, AMP strongly opposes both policies.

#### **Title, IV Subtitle S Continuing Medical Education Sunshine Exemption**

AMP is fully supportive of the inclusion of this provision which would clarify those peer-reviewed journals, journal reprints, journal supplements, and medical textbooks are excluded from the reporting requirement under the Sunshine Act. It is essential that physicians have access to the most relevant, latest emerging scientific knowledge associated with health care delivery. This legislation ensures that physicians' access to the highest quality publications in the world will remain unobstructed. Medical textbooks, consults, conference reports, journal articles and their reprints are written and published for the purpose of building upon and improving clinical understanding. These universally respected publications not only meet the rigorous standards of the highest quality peer-review and editing, but also provide impartial and independent information that provides direct benefit to patients through improved care. We believe the materials listed above are essential components to a physician's continuing medical education and this provision should be preserved in the final version of the 21<sup>st</sup> Century Cures Act.

#### **Title V, Subtitle D, Sec. 5067 Humanitarian Device Exemption Application to In Vitro Diagnostics**

AMP supports this provision which adds language to the Humanitarian Device Exemption so that an exemption can be made for IVDs used to benefit patients in the treatment of diagnosis of diseases or conditions that affect greater than 4,000 individuals in the United States annually. AMP believes the Humanitarian Device Exemption, as it is currently written, fails to adequately capture the full range of IVDs used to diagnose a rare disease or fulfill an unmet need. For example, while cancer is not considered a 'rare' or 'orphan' disease, a number of subtypes of cancer occur less than 1% of the time. Specifically, while lung adenocarcinomas have a rather high incidence, some targetable subtypes are rare and IVDs for these subtypes should be considered rare and eligible for any rare disease exemption. The Humanitarian Device Exemption provision in the 21<sup>st</sup> Century Cures Act draft removes the 4,000 limit and reaffirms that the exemption is for IVDs for diseases or conditions based on prevalence of that disease or condition, not on the number of times a test is ordered. Additionally, it allows for multiple IVDs to be granted an exemption for the same indication if the Secretary determines they are medically necessary. For these reasons, AMP recommends that this provision be included in the final version of the 21<sup>st</sup> Century Cures. We note, however, that it will be important for FDA to provide clarity on what information would be required for the Secretary to determine that the severity of the disease or condition requires greater availability of the device to treat or diagnose a disease or condition. In addition, FDA should be required to clarify what a "satisfactory alternative" would be with regards to this exemption.

AMP appreciates the opportunity to provide these comments in response to the 21<sup>st</sup> Century Cures Act discussion draft. We hope this information helps inform your efforts and that AMP can continue to work with the Committee on other sections that impact molecular pathology professionals and their patients. Please do not hesitate to contact Mary Williams, AMP's Executive Director, at [mwilliams@amp.org](mailto:mwilliams@amp.org) if we may be of assistance or provide additional information.

Sincerely,

Janina Longtine, MD  
AMP President

Additional Material:

- AMP's response to "21<sup>st</sup> Century Cures: A Call to Action":  
[http://amp.org/publications\\_resources/documents/AMPComments21stCenturyCures-ACalltoAction.pdf](http://amp.org/publications_resources/documents/AMPComments21stCenturyCures-ACalltoAction.pdf)
- Testimony submitted to Energy and Commerce for the hearing on "21st Century Cures: Examining the Regulation of Laboratory Developed Tests":  
[http://amp.org/publications\\_resources/documents/AMP.Testimony.E&C.Hearing.Regulation.LDT.2014-09-08.pdf](http://amp.org/publications_resources/documents/AMP.Testimony.E&C.Hearing.Regulation.LDT.2014-09-08.pdf)
- AMP's response to "A Modernized Framework for Innovative Diagnostic Tests":  
[http://www.amp.org/publications\\_resources/position\\_statements\\_letters/documents/AMPresponsetoECRFIfinal.pdf](http://www.amp.org/publications_resources/position_statements_letters/documents/AMPresponsetoECRFIfinal.pdf)
- MoLDx Clinical Test Evaluation Process (CTEP):  
[http://www.palmettogba.com/palmetto/MoLDX.nsf/DocsCat/MoLDx%20Website~MoLDx~Browse%20By%20Topic~General~8PKRZF3404?open&navmenu=Browse%5eBy%5eTopic|\\_|\\_|\\_|](http://www.palmettogba.com/palmetto/MoLDX.nsf/DocsCat/MoLDx%20Website~MoLDx~Browse%20By%20Topic~General~8PKRZF3404?open&navmenu=Browse%5eBy%5eTopic|_|_|_|)
- AMP's comments submitted to the docket on FDA's LDT draft guidance:  
<http://amp.org/advocacy/documents/FDAcommentsonLDTguidance-FINAL.pdf>
- AMP's white paper on *A Molecular Diagnostic Perfect Storm: The Convergence of Regulatory & Reimbursement Forces that Threaten Patient Access to Innovations in Genomic Medicine*:  
[http://amp.org/publications\\_resources/position\\_statements\\_letters/PerfectStorm.cfm](http://amp.org/publications_resources/position_statements_letters/PerfectStorm.cfm)



February 18, 2015

Congressman Fred Upton  
Chairman, Committee on Energy and Commerce  
2125 Rayburn House Office Building  
Washington, DC 20515

Dear Chairman Upton:

On behalf of the Association of Clinical Research Organizations (ACRO,) thank you for the opportunity to comment on the 21<sup>st</sup> Century Cures Discussion Document which reflects the hard work and dedication of you, Representative DeGette and your staffs on this important effort to facilitate innovation and speed the discovery, development and delivery of new biomedical products.

As the world's leading, global clinical research organizations (CROs,) ACRO member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices, from discovery, pre-clinical, proof of concept and first-in-man studies through post-approval and pharmacovigilance research. With more than 110,000 employees engaged in research activities around the world, each year ACRO member companies conduct more than 11,000 clinical trials involving nearly two million research participants.

ACRO has been very much engaged with the 21<sup>st</sup> Century Cures initiative and scientists from our member companies have testified in hearings and roundtables on modernizing clinical trials, using real-world data to inform discovery and development, and speeding vaccine development.

### **Direct Impact on Research Operations and Accelerating Development**

ACRO has been pleased to work with the Committee on three specific areas of importance to our members and the broader research community. We support the language in the following sections in current form but know that changes may be made as the bill moves through the legislative process and look forward to continued engagement on these and other issues:

Title II, Subtitle F, Building a 21<sup>st</sup> Century Data Sharing Network – Provisions in this section would raise awareness of clinical trials and greatly enhance the ability of patients and their physicians to better identify clinical trials that may be appropriate and of interest to them. We are encouraged by recent NIH actions to make [clinicaltrials.gov](http://clinicaltrials.gov) more useful and easier to navigate but believe further direction from Congress is needed. ACRO envisions a scenario in the not-too-distant future where [clinicaltrials.gov](http://clinicaltrials.gov) data is formatted in a way that it can be easily integrated into EHRs for better identification of eligible patients. Greater participation in clinical trials would vastly



accelerate the drug development process. ACRO also supports the proposals to allow further analysis of de-identified clinical trial data from selected government-funded research projects and to establish a Commission on Data Sharing for Research and Development.

Title II, Subtitle M, Accessing, Sharing and Using Health Data for Research Purposes – ACRO strongly supports revision of Health Insurance Portability and Accountability Act (HIPAA) regulations that impede the use of health data for research purposes. We applaud your proposals to loosen the current constraints on data access, sharing and use that have resulted in data “silos” and a lack of interoperability among and between the clinical research and clinical care spheres. We believe that the changes proposed would facilitate responsible use of health care data for the betterment of patients and improvement of the health care system, while carefully protecting the confidentiality and privacy of individuals.

Title III, Subtitle A, Clinical Research Modernization Act – ACRO has long advocated for a streamlining of the Institutional Review Board process for multicenter clinical trials. This provision alone could reduce the time to develop a new drug by several months, bringing benefits to patients in need much sooner.

### **General Comments**

ACRO is very supportive of the goals of 21<sup>st</sup> Century Cures, especially efforts to streamline the clinical trials process, accelerate the discovery and development of new medical products, modernize medical product regulation and engage patients more broadly in the development and regulatory processes.

At the same time, we do have some concerns that several of the provisions designed to accelerate the development process could place a strain on regulatory resources, necessitate additional funding for basic research, regulatory science and highly-skilled regulatory staff, and have the potential to diminish regulatory discretion. To the extent the Food and Drug Administration would be given additional responsibilities, we urge Congress to simultaneously provide additional appropriations for the FDA to carry out an expanded mission. We believe the current ratio of appropriations to user fees should be maintained in the interest of sound public policy and regulatory independence.

While the primary focus of ACRO’s members is in the area of drug development, we also have an interest in medical device research. As such, we will provide a general comment on the various device, diagnostic and combination product provisions. We note several provisions in this draft document propose a variety of accelerated or “breakthrough” pathways for devices. With a trend toward more combination drug-device products and the increased use of companion diagnostics, we support efforts to bring some areas of device regulation into parity with that of drugs to enable a predictable regulatory approval pathway. We encourage the Committee to consolidate its approach to modernizing the regulatory structure for devices.

## **Specific Comments – Title I**

Subtitle A – Patient Focused Drug Development – ACRO supports this provision and encourages the Committee to incorporate meaningful metrics to evaluate the impact of patient engagement on the development process.

Subtitle B – Surrogate Endpoint Qualification and Utilization – ACRO supports the development of scientifically valid surrogate endpoints and the use of public-private partnerships to qualify other types of biomarkers. Our members are highly engaged in these efforts currently.

Subtitle C – Approval of Breakthrough Therapies – ACRO is concerned that the use of “early stage clinical data” may often be insufficient to make decisions to approve a new drug. Numerous studies have shown that between 40 percent and 50 percent of compounds fail in Phase III studies, so approving a new drug with only Phase II data presents considerable risk. Further, in a 2013 member survey, we found that ACRO members conducted 2,172 Phase II trials with a median patient population of only 92 participants. We question whether data from less than 100 people is sufficient for broad approval of a new medical product (rare diseases excepted,) even with required post-market assessment. In order to preserve credibility and independence, the FDA must maintain the flexibility to determine the appropriate amount of clinical data needed to make an approval decision. The current breakthrough therapy designation has provided great benefits to patients and the industry. Efforts must be made to ensure these therapies are truly “breakthrough” and are addressing serious and life threatening conditions. We must maintain a sound benefit-risk assessment framework to ensure patient safety and maintain an adequate regulatory apparatus. As suggested in this discussion draft, a broader examination of clinical trial practices concerning the use of surrogate endpoints, biomarkers, adaptive trial designs and Bayesian statistics is warranted and welcomed. We must find ways to accelerate the development of new medical products. But with current practices, relying solely on Phase II clinical trial data for approval could lead to negative outcomes for patients.

Subtitle D – Antibiotic Drug Development – ACRO is supportive of efforts to encourage the development of new antibiotics, including the use of adaptive trial designs.

Subtitle I – Modernizing the Regulation of Social Media – FDA guidance on social media use by the biopharmaceutical industry has been inadequate to date. While this is a difficult and ever-changing landscape to negotiate, more regulatory guidance and certainty are needed. We also recommend the FDA provide guidance around the acceptable use of social media for clinical trial recruitment.

Subtitle J – Streamlined Data Review – ACRO is concerned that in many cases data summaries may be inadequate for adding indications to a drug label. Again, the FDA must maintain the flexibility and authority to establish appropriate data parameters for adding new indications. In some cases, the data summaries may provide overwhelming

evidence that new indication is warranted, but in others it may simply indicate additional research and data are required.

Subtitle K – Cures Acceleration Network – ACRO strongly supports efforts to enable NCATS to operate more like DARPA. Our members have been frustrated in attempts to bring our private sector efficiencies to NCATS.

Subtitle L – Dormant Therapies – ACRO has been on record in support of the MODDERN Cures Act and similar efforts to promote the development of dormant therapies.

## **Specific Comments – Title II**

Subtitle A – 21<sup>st</sup> Century Cures Consortium Act – ACRO supports the establishment of this public private-partnership and notes that the European Union’s Innovative Medicines Initiative on which it is based, in part, currently has a 10-year budget of approximately \$3.8 billion.

Subtitle B – Medical Product Innovation Advisory Council – ACRO supports the creation of the Commissions and believes our members could be valuable contributors to its mission.

Subtitle C – Regenerative Medicine – ACRO is generally supportive of efforts to foster development of a clear, predictable regulatory pathway to enable speedy approval of safe and effective regenerative medicine products.

Subtitle D – Genetically Targeted Platform Technologies for Rare Diseases – ACRO supports efforts to direct the FDA to develop clear and predictable regulatory pathways for new technologies that address unmet medical needs, such as the case of rare diseases.

Subtitle E- Sensible Oversight for Technology Which Advances Regulatory Efficiency – ACRO is generally supportive of the SOFTWARE Act.

Subtitle F – Building a 21<sup>st</sup> Century Data Sharing Framework – As previously mentioned, ACRO strongly supports a new data sharing framework, utilizing widely-recognized data standards, to better enable patients and physicians to identify opportunities to participate in clinical trials.

Subtitle G – Utilizing Real-World Evidence – ACRO believes that, within limits, there are tremendous opportunities for the use of real world evidence and would welcome FDA guidance on its collection and potential uses. The FDA must retain the authority to determine when, and to what extent, real world evidence presents a sufficient basis to make regulatory determinations.

Subtitle H – Coverage with Evidence Development – ACRO is generally supportive of this measure.

Subtitle M – Accessing, Sharing and Using Health Data for Research Purposes – As mentioned previously, ACRO is very supportive of efforts to modernize HIPAA to encourage greater use of health data for research purposes while maintaining patient privacy.

Subtitle N – 21<sup>st</sup> Century Chronic Disease Initiative Act – ACRO strongly supports requiring HHS to carry out a longitudinal study of patients with chronic disease to improve health outcomes and generate important research findings.

### **Specific Comments - Title III**

Subtitle A – Clinical Research Modernization Act – As previously mentioned, ACRO supports efforts to streamline the IRB process and accelerate the pace of multicenter clinical trials without compromising patient safety. We believe that in some cases, single IRB approval could be made a requirement in order for sites to participate in research programs undertaken under a Breakthrough Therapy designation.

Subtitle B – Broader Application of Bayesian Statistics and Adaptive Trial Designs – ACRO members are leaders in designing and implementing new clinical trial designs and strongly support this provision. To be most effective, we ask the Committee to direct the FDA to implement and administer enforceable development plans to prevent against regulatory confusion during the course of a trial.

Subtitle D - Pediatric Research Network Improvement and Subtitle E – Global Pediatric Clinical Trial – ACRO members have already created global networks of qualified, high-quality investigators and research sites in the area of Pediatrics. The NIH should make every effort to engage these private-sector networks before starting from scratch to build their own network.

### **General Comments - Title IV**

An argument can always be made for additional funding for basic research at the NIH. In general, ACRO supports additional government investment in research. We also fully recognize the budget constraints faced by Congress. We believe a number of the provisions in Title IV could necessitate additional funds for NIH. At the same time, we believe a number of the accountability and planning provisions could lead to savings that would have the net effect of an increase the NIH research budget. Similarly, if NIH-sponsored clinical trials were to avail themselves to the efficiencies of outsourcing of non-core functions, such as project management, data management and data analysis, additional funds would be freed up for research investment. There is no reason the NIH should not take advantage of the same private sector research expertise the biopharmaceutical industry employs to increase efficiency and lower cost.

## **Specific Comments -Title IV**

Section 4009 – NCATS Phase IIB Restriction – ACRO favors removal of this funding restriction and again encourages NCATS to work more closely with private research companies in the conduct of Phase IIB clinical trials.

Subtitle C – Vaccine Access, Certainty and Innovation – ACRO members are currently involved in the development of more than 100 vaccines for therapeutic areas ranging from influenza and chickenpox to oncology and Alzheimer's. As such, we strongly support efforts to accelerate innovative vaccine development.

Subtitle D – Reagan- Udall Improvements - ACRO supports improvements to the Reagan-Udall Foundation to better assist the FDA with complex scientific and operational issues.

Subtitle F – FDA Succession Planning – From experience, ACRO believes the industry (and, ultimately, patients) benefits from consistency and expertise at the senior levels of management at the FDA. As such, we support succession planning.

## **Specific Comments - Title V**

Section 5061 – Third-party quality assessment system – ACRO supports allowing the FDA to relay on accredited third-parties to certify minor manufacturing changes.

Section 5062- Valid scientific evidence – ACRO supports the recognition of the value of real world evidence but recommends the judicious use of real world evidence in regulatory actions.

Thank you for the opportunity to comment. We look forward to the opportunity to work with the Committee and with the Senate as the Cures initiative progresses.

Respectfully Submitted,



Doug Peddicord, Ph.D.  
Executive Director

Hi Clay, John, Carly, Paul and Robert,

On behalf of AstraZeneca, we would like to reiterate our appreciation that the Committee has included many of the topics addressed in our written recommendations in the 21<sup>st</sup> Century Cures Act discussion draft. We believe that the 21<sup>st</sup> Century Cures initiative will advance innovation and make a difference in the lives of patients. As the Committee moves forward, we offer the following comments for your consideration.

**Surrogate Endpoint Qualification and Utilization** (sections 1021-1024). While we appreciate the proposed enhancements to the qualification process, we are concerned that the scope of the provisions may be too narrow as the provisions are limited to surrogate endpoints. Validated biomarkers can be used in a wide range of other important applications, including, for preclinical and clinical safety and efficacy uses. These uses can substantially accelerate product development timelines and ensure safer medicines for patients. Thus, the need exists for a predictable, evidence-based, and timely process for qualification of all biomarkers. For these reasons, we recommend that the Committee expand the scope of sections 1021-1024 to include all biomarkers.

We have a specific comment on the composition of the public forum proposed in the qualification provisions (page 21, line 10 – page 22, line 12). We suggest including in the forum one or more technology development experts (for example, experts in assay technology platforms). Technology underlies the biomarker (analytical) validation which is essential for qualification, and including expert representatives in the public forum will help to ensure regulatory decisions are made on the basis of the most complete and up-to-date information.

We further note that the draft contains provisions to address pending requests for biomarker qualification (section 1023). Again, we are concerned that the scope of the provisions may be too narrow as it is limited to requests for the qualification of a biomarker as a surrogate endpoint. We understand that many pending requests address other types of important biomarkers, and we recommend that the Committee consider constructing a formal process for the qualification of those biomarkers.

**Clinical Trial Modernization** (section 3021). We applaud the inclusion of provisions addressing clinical trial modernization. As we noted in our written recommendations to the Committee, in some cases different approaches to clinical trials – beyond the traditionally required three phases of large scale, controlled trials – may be appropriate. We therefore appreciate the proposals set forth in section 3021. Our comment for consideration relates to the “Review and Revision of Guidance Documents” provisions. Given the pace with which scientific advances in biomedical research occur, we recommend that the Secretary include key external experts and stakeholders in the review and revision of the guidance documents on adaptive trial design and Bayesian methods. This could be achieved through a public meeting with relevant stakeholders or through another consultation process. We believe such engagement would help raise awareness of the evolving science and help improve the efficiency of the regulatory decision-making process.

**Postapproval Studies and Clinical Trials** (section 3031). We are likewise pleased to see that the Committee addressed the issue of evaluating postapproval studies and clinical trials. We believe the Committee should clarify that only the sponsor may request an evaluation of a postapproval study or clinical trial under this section. We have one technical comment on page 236, lines 14-15. As proposed, the section describes the process by which the Secretary must periodically evaluate a postapproval

study or clinical trial to determine whether “the design, or the timelines applicable to the completion of, the study or trial should be renegotiated *because of changes in medical practice or the standard of care.*” (emphasis added). We believe that this section might be too narrowly drafted and could be read to limit the acceptable reasons for renegotiating the design or timelines applicable to the study or trial. Other legitimate circumstances could exist that might necessitate a renegotiation of the design or timelines, for example, practical feasibility issues with respect to timeframes. Thus, we encourage the Committee to expand this provision to account for other reasons for renegotiating the design or timelines.

**Utilizing Real World Evidence** (section 2101). We support the inclusion of the provision, “Utilizing Real World Evidence” and believe that guidance in this area will be extremely helpful. One comment for the Committee’s consideration is to include a specific reference to the PCORI methodology report (see <http://www.pcori.org/assets/2013/11/PCORI-Methodology-Report.pdf>, accessed February 10, 2015). This report has been fully vetted and could serve as a basis for standards associated with patient centeredness, data registries, and data networks.

**Combination Products** (sections 2141-2142). We support the concepts included in the Combination Products provisions. It is vital for project teams to understand who the lead review center will be and to have a consistent point of contact during the regulatory review process.

**Facilitating Responsible Communication of Scientific and Medical Developments** (section 1141). As you are aware, our written comments to the Committee recommended that the Committee clarify the scope of permissible communications with payers prior to the launch of a new medicine. We are pleased to see that the Committee intends to clarify and rationalize rules associated with communication of scientific and medical developments between physicians, insurers, and researchers. We continue to have a particular interest in this topic and stand ready to work with the Committee on this issue.

Thank you for the opportunity to review this draft legislation. We look forward to continued engagement with the Committee on this and commend you for all of your hard work in crafting this draft legislation.

Sincerely,  
-Theresa

**Theresa Jolivette, J.D.**

Director, Federal Government Affairs

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February 10, 2015

The Honorable Fred Upton  
Chairman  
House Energy and Commerce Committee  
U.S. House of Representatives  
2125 Rayburn House Office Building  
Washington, D.C. 20515

The Honorable Diana DeGette  
Member  
House Energy and Commerce Committee  
U.S. House of Representatives  
2125 Rayburn House Office Building  
Washington, DC 20515

Dear Chairman Upton and Representative DeGette:

I write again on behalf of the millions of American children and adults affected by autism, their families and caregivers, and the entire team at Autism Speaks, to thank you for undertaking the 21<sup>st</sup> Century Cures Initiative. This initiative is welcomed by those in our community who seek game-changing progress in medical treatment. Investment in developing treatments for central nervous system (CNS) disorders, like autism, is critically lacking because of the risk profile for such investments. Autism Speaks primary goal for this initiative is to drive CNS investment through sensible regulatory reforms that better define the risk for research and investment in this field.

As you know, Autism Speaks has undertaken a historic project with Google to foster innovation and research in autism through the sequencing of ten thousand whole genomes. The lead investigators for this project, called MSSNG, recently published a major research finding in *Nature Medicine* that showed siblings with autism often have different autism-linked genes. The open-science data set that resulted in this publication portends the day of personalized medicine desired from the 21<sup>st</sup> Century Cures initiative. This initiative should result in a framework that encourages more investment in medical innovation to capitalize on the exciting progress we are making.

#### **Recommendations:**

As you also know from our November 2014 submission, Autism Speaks associated itself with many of the recommendations made by the American Brain Coalition (ABC), of which we are a member. In addition, we have identified several areas of importance from the discussion draft beyond ABC's submission:

**Title I: Subtitle B, Surrogate Endpoints** – As noted in our November submission, the ability to utilize surrogate endpoints as predictors of clinical benefit has great potential in autism research. We are gaining important insight into autism as genetic and imaging technologies mature. This is an emerging area and the regulatory regime should support these developments. The FDA should be receptive to biomarker and other surrogate endpoint discovery that can assist in predicting clinical benefit. Stakeholders should be able to collaborate with FDA on developing and validating innovative outcome measures.

**Title I: Subtitle C, Approval of Breakthrough Therapies** – Autism presents a critical unmet need because there is no treatment for its core symptoms. We support this provision which





clarifies that FDA may use a breakthrough designation and consider approval based on early stage clinical data for conditions with unmet medical needs. Early stage clinical data is not appropriate for every disease or condition, but for those like autism, without options, it could be beneficial. Further, we encourage you to better define “unmet medical need” to recognize the unique opportunities for disease modification in children and their great unmet needs.

**Title I: Subtitle L, Dormant Therapies** –We believe complex diseases need incentives for private investment. Allowing investigators to choose new pathways for dormant therapies targeting complex diseases and receive a fixed year protection upon FDA approval would provide such an incentive.

**Incentives** – The discussion draft provides incentives in several areas (Subtitle L, Dormant Therapies, Subtitle M, New Therapeutic Entities, and Subtitle N, Orphan Product Extensions Now). However, we would encourage the committee to be bolder in the area of CNS investment. Because the investment is so lacking and the need is so great, CNS development is in particular need for incentives. Our suggestion within the committee’s jurisdiction is to utilize the enterprise zone model for CNS investment to create Medical Research Enterprise Zones. These zones could be created around significant research hospitals and universities to speed the ability to cure a range of CNS disorders. They could include accelerated regulatory processes that would attract significant new private sector research funds. This model would allow states to amplify the federal effort by creating their own incentives or removing burdens to investment. Competition among the states would facilitate and incentivize innovation.

**Patient Reported Outcomes** – The discussion draft does not clearly identify PRO as an area of interest. Encouraging the scientific study of PRO, the inclusion of PRO in pivotal clinical trials, and validated PRO as the basis for approval by FDA would greatly assist efforts to discover and develop new treatments.

**FDA Advisory Committee specialization** – We strongly encourage you to review the advisory committee process to ensure that proper expertise and specialization is represented. It is not clear that the discussion draft reflects this need.

**Flexible and rational interpretation of data** – We are learning much about the genetic composition of autism. We have learned that there are many subsets of autism that could be quite rare and be receptive to treatment. Flexibility by the FDA to consider how subgroups react to clinical trials could greatly accelerate new treatment.

## Conclusion

Once again, we applaud your efforts underway to help facilitate medical innovation. We look forward to assisting you in this initiative to ensure its promise is fulfilled.

Sincerely,

Liz Feld  
President

February 10, 2015

The Honorable Fred Upton  
Chairman  
Energy & Commerce Committee  
U.S. House of Representatives  
2125 Rayburn House Office Building  
Washington, DC 20515

**Re: Section 4141 of 21<sup>st</sup> Century Cures Discussion Draft; Proposed Amendment to Address the Harmful Effects of CMS's "MLR" for DME on Innovation of Class III Medical Devices**

Dear Chairman Upton:

On behalf of the Bone Growth Stimulator ("BGS") Coalition, we applaud the efforts of the House Energy & Commerce Committee's 21<sup>st</sup> Century Cures Initiative. The BGS Coalition, comprised of industry leaders including DJO Global, Inc., Biomet Bone Healing Technologies, Orthofix International N.V., Bioventus LLC, and EMSI fully supports the Committee's goal of encouraging the development of new and innovative medical treatments. We write today to comment on Section 4141 of the Committee's Discussion Draft, to urge the Committee to amend the provision to exempt Class III medical devices from the Centers for Medicare & Medicaid Services ("CMS") requirement that durable medical equipment ("DME") meet a vague and impractical three-year minimum lifetime requirement ("MLR").

The BGS Coalition represents over 60 years of experience with BGS devices and manufactures all of the BGS devices that are currently reimbursed by the Medicare program as DME. As explained below in more detail, CMS covers existing BGS devices, but has radically complicated Medicare beneficiary access to new and emerging BGS technologies, and even improvements of existing technology, through its uncertain MLR requirement, which appears to impose a three-year durability requirement for even the most mundane improvements to existing technology. To resolve these issues, we urge the Committee to amend the definition of DME in Section 1861(n) of the Social Security Act as follows:

*(a) In general – Section 1861(n) of the Social Security Act (42 U.S.C. 1395x(n)) is amended by adding at the end the following sentence:*

*“With regard to an item that—*

*(1) would be classified as ‘durable medical equipment’ except for the failure to satisfy an applicable minimum lifetime requirement established by the Secretary and*

*(2) is a class III device under the Federal Food, Drug, and Cosmetic Act*  
*such item shall be classified as ‘durable medical equipment’.*

*(b) Effective Date – The amendments made by subsection (a) shall take effect as of January 1, 2012.*

This is not the first time that Congress would exempt Class III devices from new policies altering longstanding DME reimbursement. In 2003, Congress exempted Class III devices from the DME Competitive Bidding Program. Social Security Act § 1847(a)(2)(A). Congress should do the same here, and exempt Class III devices from the MLR to promote innovation and protect the health of Medicare beneficiaries, a goal that falls squarely within the mission of the 21<sup>st</sup> Century Cures Initiative.

**Why is this change needed?** Effective January 1, 2012, CMS revised the definition of DME, adding a three-year MLR that products must satisfy to be eligible for reimbursement under the Medicare DME benefit category. The MLR only applies to “new” products classified as DME after January 1, 2012. Any items classified as DME prior to that date are “grandfathered”, and continue to be eligible for reimbursement, regardless of whether or not they can withstand 3 years of use. Further, as long as a grandfathered item is only “modified” or “upgraded” after January 1, 2012 and is not considered a brand “new” product by CMS, it would continue to fall within the grandfathering provision and would not need to meet the MLR.<sup>1</sup>

In response to numerous inquiries from Members of Congress and the public,<sup>2</sup> CMS subsequently attempted to provide additional guidance on how CMS defines “grandfathered” and “new” products. Specifically, a “grandfathered item that is modified (upgraded, refined, reengineered, etc.), is still considered a grandfathered item rather than a new item, unless the item is less durable, such that it now has an expected life that is shorter than the expected lifetime for the [original grandfathered item].” A “grandfathered” product is “a specific product (make, manufacturer, model, model number, etc.) that was covered and paid for as DME on or prior to January 1, 2012.” A “new” product is one “that was not paid for as DME on or prior to January 1, 2012, or a grandfathered item that loses its grandfathered status.”<sup>3</sup>

Even with this subsequent “clarification,” CMS has failed to provide sufficient guidance regarding to what *degree* changes can be made to a grandfathered DME product before it is no longer considered a “modified” or “upgraded” product, but a brand “new” product, and therefore, no longer covered by Medicare as DME. As it currently stands, DME manufacturers cannot reliably determine whether a product seeking coverage under the DME benefit after January 1, 2012 can even be compared to a “grandfathered” product, or is simply a “new” product that can never be subject to the grandfathering provision. A clear understanding of the framework that CMS will use to analyze these issues is essential to DME manufacturers seeking to transform their technologies, incrementally or substantively, in ways that rise to meet the evolving needs of Medicare beneficiaries to improve patient experience and enhance health outcomes. As a result of this new policy, DME manufacturers are reluctant to update and improve their products for fear of losing Medicare coverage.

This effect is particularly acute in the case of stimulation devices that activate the biochemical mechanisms that govern cellular growth and repair, such as BGS devices, approved as Class III (PMA) devices by the Food and Drug Administration (“FDA”). With sizable R&D risk and investment costs

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<sup>1</sup> 76 Fed. Reg. 70228 (Nov. 10, 2011) (emphasis added).

<sup>2</sup> Since 2011, Members of Congress have sent multiple letters to the Secretary of Health and Human Services and Administrator of CMS on the MLR issue. These include: Letter dated October 17, 2013 to Secretary Sebelius (signed by Reps. Blackburn, Burgess, Harper, Latta, Stutzman); Letter dated June 8, 2012 to (Acting) Administrator Tavenner (signed by Sens. Burr, Coburn, Cornyn, Crapo, Enzi, Hatch, Kyle, Roberts, Thune); Letter dated May 29, 2012 to (Acting) Administrator Tavenner (signed by Sen. Kerry); Letter dated May 4, 2012 to Secretary Sebelius (signed by Reps. Bilbray, Black, Blackburn, Buchanan, Burgess, Ellmers, Harper, Latta, Myrick, Sullivan); Letter dated December 9, 2011 to Secretary Sebelius (signed by Reps. Black, Blackburn, Bilbray, Burgess); Letter dated November 8, 2011 to Acting Administrator Berwick (signed by Sens. Burr, Cornyn, Crapo, Coburn, Enzi, Grassley, Hatch, Kyl, Roberts, Snowe, Thune); Letter dated October 14, 2011 to Secretary Sebelius (signed by Reps. Altmire, Bilbray, Black, Blackburn, Burgess, Ellmers, Harper, Latta, Myrick, Neal, Roskam, Sullivan).

<sup>3</sup> 78 Fed. Reg. 72156 (Dec. 2, 2013) (emphasis added).

present in the development of medical device enhancements, and as a consequence of the lack of general principles allowing manufacturers to infer whether or not a reasonable chance exists that a device will continue to be reimbursed as DME when innovations are pursued, companies are unable to secure necessary approval and funding to pursue projects focused on addressing healthcare challenges associated with a high-risk, ever-increasing, elderly Medicare population. The MLR and its vague grandfathering provision stifle innovation of BGS devices in the following ways:

- BGS device manufacturers hesitate to make even slight modifications to their existing devices (e.g., different garment covering, revised switches or display casing) for fear that they will no longer be reimbursed as DME. **What extent of modifications can occur before a BGS device is no longer “modified” but “new” and thereby not DME?**
- The underlying electrical or ultrasound technology in BGS devices that is used to stimulate cellular growth or repair is currently being explored for use as a non-invasive, cost-effective treatment for different indications prevalent in the Medicare beneficiary population (e.g., osteoarthritis, repair of damaged cartilage caused by osteoarthritis, healing of diabetic foot ulcers). It is possible that existing BGS devices may be approved by FDA for different indications without any physical changes to the BGS devices themselves. Manufacturers are reluctant to invest in the clinical trials and other research to investigate these different indications if there is no way to determine whether the device will be reimbursed as DME. **Is an existing BGS device approved for a different indication a “modified” device or a “new” device?**
- At least one company does not currently have a BGS device on the market but plans to launch a BGS device in the future. If CMS does not consider this BGS device to be DME, then CMS would create significant barriers to entry into the market for creative technological innovations by newcomers to the industry. **Will BGS devices entering the market be considered “new” devices (not DME) or “modified” versions of existing BGS devices (eligible for reimbursement as DME)?**

**The Solution: Exempt Class III Devices from the MLR.** Despite multiple requests, CMS has repeatedly declined to issue clear, written guidance that protects and promotes the ability of DME manufacturers to innovate their products to meet the evolving needs of Medicare beneficiaries. Therefore, Congress should address this significant issue through legislation. Given that CMS’s failure to issue clear guidance on the grandfathering provision of the MLR is particularly acute for Class III (PMA) devices, where there is high burden associated with substantial R&D risk and investment costs necessary to develop enhancements and innovations, **Congress should exempt Class III devices from the MLR.** Although the proposed new Medicare benefit category of “substitute disposable medical technology” in Section 4141 of the Discussion Draft is an important step forward in assuring Medicare coverage for certain new and innovative technologies that may not be considered “durable” by CMS, it does not sufficiently protect Medicare coverage for potential innovations to Class III devices. For such devices, where substantial time and resources are expended for enhancements and improvements to meet the evolving needs of Medicare beneficiaries, CMS may nevertheless determine that such devices fall outside both the DME and the “substitute disposable medical technology” Medicare benefit categories, leaving such innovative technologies with no Medicare coverage. For this reason, we strongly urge the Committee to amend Section 4141 to exempt Class III medical devices from the MLR.

\* \* \*

Thank you for your consideration. We look forward to discussing our proposal further with you. In the meantime, should you have questions or need additional information, please contact us at (202) 626-5547.

Sincerely,

  
A large black rectangular redaction box covers the signature. Below the box, a handwritten mark resembling a cursive 'J' or '0' is visible.

Preeya Noronha Pinto  
David J. Farber  
William Clarkson

*Counsel for the BGS Coalition*

Attachment

## ATTACHMENT

### Background on Bone Growth Stimulator Devices

Bone Growth Stimulator (“BGS”) devices, also known as osteogenic stimulation devices, were first approved as Class III devices by the Food and Drug Administration (“FDA”) in the mid-1980s. Since that time, the Centers for Medicare & Medicaid Services (“CMS”) has recognized and reimbursed these devices as durable medical equipment (“DME”) in the Medicare program.

Electrical BGS devices consist of electrodes or electromagnetic coils encased in pads that are attached to an external power supply and placed over a cast or directly on the skin. The external power supply and externally applied coils transmit an electrical current to the fracture or fusion site via pulsed electromagnetic fields, combined electromagnetic field technology, or capacitive coupling to stimulate fracture healing and fusion. Ultrasound BGS devices emit low intensity, pulsed ultrasound. The devices are applied to the surface of the skin at the fracture or fusion site, and ultrasound waves are emitted via a conductive coupling gel to stimulate fracture healing or fusion.

The following are depictions of various models of BGS devices:



For over thirty years, BGS devices have been provided to high-risk patients pursuant to an authorized prescription from a treating physician to help promote healing and bone fusion for a number of different indications. These indications include:

- Treatment of non-union fractures (i.e., long/short bone fractures that are not healing)
- Adjunct to spine and cervical fusion surgeries to lower the risk of pseudarthrosis (i.e., false joint or incomplete bridging of bone fusion segments)
- Treatment for established pseudarthrosis (e.g., unsuccessful spinal or cervical surgeries in high-risk patients where vertebral sections fail to fuse after surgery).

In general, the patient administers treatment at home once daily, for an extended period of time as prescribed by a physician. Treatment continues until the fracture is sufficiently healed or the fusion site is completely bridged, as determined by a treating physician. Utilization of BGS devices has resulted in higher fusion success rates and has reduced the need for surgical revision procedures. As such, BGS devices have improved patient outcomes and decreased healthcare costs.

February 11, 2015

The Honorable Fred Upton, Chairman  
House Energy & Commerce Committee  
2125 Rayburn House Office Building  
Washington, DC 20515

The Honorable Diana DeGette  
House Energy & Commerce Committee  
2125 Rayburn House Office Building  
Washington, DC 20515

Dear Chairman Upton and Representative DeGette,

California Healthcare Institute (CHI), the statewide public policy organization representing California's leading biomedical innovators – comprised of over 275 research universities and nonprofit institutes, venture capital firms, and medical device, diagnostic, biotechnology and pharmaceutical companies – appreciates the opportunity to present its views in response to the Committee's landmark "21st Century Cures" initiative (Initiative) discussion draft.

#### Overview

Since our founding in 1993, CHI's mission has been to advocate for policies that promote and advance California's biomedical innovation ecosystem and the benefits it brings to our economy and, most important, patients in need around the world. Over these two decades, we have worked to address a wide range of issues, including science research, FDA regulatory processes, and coverage and payment policies. And during this time, our mantra has been that truly fostering a healthy and vibrant biomedical ecosystem requires getting policies right across each of these and other areas -- together. That is why, first and foremost, we want to recognize and applaud your leadership in launching the 21<sup>st</sup> Century Cures Initiative, which is the first time that Congress has approached the full progression of biomedical discovery, development and delivery in such a comprehensive and visionary manner, with input from and collaboration with a far-ranging set of stakeholders.

With the release of the Initiative's discussion draft, CHI welcomes the opportunity to provide feedback that we hope will be informative to advancing your work. We have organized our responses into three sections: 1) Provisions that reflect our original "discovery"-focused recommendations; 2) Provisions that reflect other measures and policies we have supported outside the scope of our submitted recommendations; and 3) Other provisions in the discussion draft of significant importance to CHI and the sector we represent.

#### Provisions that reflect CHI's original "discovery"-focused recommendations

Recognizing the significant input others were offering with respect to the "development" and "delivery" elements of the Initiative, CHI's formal comments to the committee were particularly focused on "discovery," especially as they pertain to science research and the National Institutes of Health (NIH). And we were pleased that the Committee's discussion draft included or reflected a number of our proposals:

- To reduce the administrative and regulatory burdens on scientific productivity, CHI proposed a formal "evaluation of proposals to restructure, streamline and simplify NIH grant proposal submission and progress report requirements, plans to implement any such proposals, and options for Congress to provide any necessary legislative or regulatory authority which may be required to implement such plans." **The discussion draft includes a provision (Section 4002) that would establish and implement just such an undertaking, which we strongly support.**

- Existing regulations and policies restrict the ability of federally funded scientists to participate in and travel to scientific conferences, hindering public-private engagement and peer-to-peer collaboration. According to the NIH, overseeing the request, review, and approval process for researcher travel requests alone costs the Agency over \$14 million per year and requires 156 full-time employees, often causing the agency to miss opportunities for early and less expensive conference registration costs. Additionally, the National Science Board found that compliance with travel requirements was among the most frequently cited burdens reported by researchers and institutions. CHI urged the Committee to develop a more flexible travel policy for biomedical researchers funded by the Public Health Service. **The discussion draft includes a placeholder provision (Section 4003) on this issue, suggesting the recommendation is under consideration but still in development, which we strongly support and are appreciative of.**
- Prior to enactment of the National Institutes of Health Reform Act of 2006, Congress had gone 13 years without comprehensive analysis of the NIH's 27 Institutes and Centers and how these entities were working together toward the vital role of advancing biomedical research. With more than eight years having passed since Congress took a comprehensive look at NIH, CHI recommended consideration of a five-year strategic plan that focuses on reevaluating current NIH programs and policies to enhance current and future biomedical research and related priorities. **The discussion draft includes a provision (Section 4001) to require NIH to work with researchers, patient advocacy groups, and industry leaders to develop and maintain such a 5-year biomedical research strategic investment plan, a provision we strongly support.**
- Echoing a theme repeated in many of the Initiative's hearings and roundtables, CHI joined in calling for thoughtful proposals to invest in a new generation of biomedical scientists. **The discussion draft includes a provision (Sections 2261) that would supplement current funding for emerging scientists in their field by allocating additional dollars from the NIH Common Fund for this purpose, a goal which we strongly support.**

Provisions that reflect other measures and policies we have supported outside the scope of our submitted recommendations

In addition to the discovery-related proposals included in our original recommendations letter, CHI is pleased that the discussion draft includes other measures that we have publicly supported, and laud the Committee for considering them as part of the Initiative. In particular:

- Antibiotic Drug Development (Title I, Subtitle D)

CHI has endorsed legislation – The Antibiotic Development to Advance Patient Treatment (ADAPT) Act and the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms (DISARM) Act – that follows-on the successful enactment of the 2012 Generating Antibiotic Incentives Now (GAIN) Act. Together, ADAPT and DISARM supplement GAIN's FDA-related reforms and further enhances regulatory and payment mechanisms key to sustaining and bolstering critical antimicrobial research and development. We strongly support the inclusion of these measures in the Initiative. Further, we applaud the Committee for considering thoughtful and creative approaches to further stimulate product development, continued antimicrobial-related research at the National Institutes of Health (NIH) and programs to support patient access to needed medications and treatments.



- Dormant Therapies (Title I, Subtitle L)

CHI has endorsed the MODDERN Cures Act, and thanks the Committee for including in the Initiative discussion draft provisions to foster and reward research and development in areas of unmet medical needs through the establishment of a “dormant therapy” pathway at the FDA.

- Orphan Products (Title I, Subtitle N)

CHI has endorsed the Orphan Product Extensions Now (OPEN) Accelerating Cures & Treatments Act, which is the basis for this provision, and applauds its inclusion in the Initiative.

- Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative (Title IV, Sec. 4008)

CHI strongly supports the BRAIN initiative, and is pleased to note that complementary work has also been supported at the state level in California. We applaud the Committee for inclusion of this provision in the Initiative draft.

- Medical Testing Availability (Title IV, Subtitle T)

CHI has previously endorsed legislation to clarify the law regarding Research Use Only (RUO) products, and thanks the Committee for including this provision in the Initiative draft.

- Medical Device Reforms (Title V, Subtitle D)

CHI is on-record in term of supporting a number of improvements to medical device-related regulatory mechanisms, including third-party quality system assessment (Sec. 5061), clarification of valid scientific evidence (Sec. 5062), reinforcement of the “least burdensome” concept (Sec. 5063), humanitarian device exemption (HDE) flexibility and application to diagnostic technologies (Sec. 5067), and improving and streamlining the advisory committee process (Sec. 5068). We applaud the Committee for including these regulatory reforms in the Initiative.

Other provisions in the discussion draft of significant importance to CHI and the sector we represent

In addition to provisions that reflect either CHI’s formal Initiative recommendations or other measures we have publically supported, the discussion draft includes a number of provisions we would also like to highlight for support. And, again, we applaud and recognize the thoughtfulness of your work in developing and considering such provisions.

- Breakthrough Devices (Title I, Subtitles E and F)

CHI was strongly supportive of the Breakthrough Therapy designation and related accelerated review processes instituted as part of the FDA Safety and Innovation Act (FDASIA). To date, these mechanisms have proven extremely beneficial to industry and patients alike, illustrating that we can have both rigorous science and safety standards *and* efficient, expedited and predictable review processes. CHI is very supportive of proposals that would establish similar mechanisms for breakthrough medical devices, such as included in the Initiative discussion draft. We are in communication with our device membership on these particular provisions and

will be pleased to share any specific feedback we receive from them as the Initiative moves forward, and we again applaud and support the Committee for including this in the discussion draft.

- Facilitating Responsible Communication of Scientific and Medical Developments (Title I, Subtitle H)

CHI is supportive of and encouraged by the Committee's intent to include a provision to update the FDA's existing rules and policies governing what drug and device manufacturers may communicate around uses of their own products. Recognizing the need for important protections to ensure that such information is truthful and non-misleading, policies should not limit the ability of providers, payers and patients to access a robust body of evidence that will allow them to make the most appropriate clinical decisions. We applaud the Committee for thoughtfully considering this important issue as part of the Initiative.

- Cures Acceleration Network (Title I, Subtitle K)

CHI has been supportive of the efforts of the National Center for Advancing Translational Science (NCATS), and appreciates the Committee's inclusion of provisions that would strengthen and bolster their work, including in the area of repurposing drugs for new uses.

- 21<sup>st</sup> Century Cures Consortium (Title II, Subtitle A)

CHI is particularly supportive of proposals that would foster public-private partnerships across the biomedical discovery, development and delivery processes. Noting this, we are very pleased that the discussion draft includes the establishment of a formal consortium of government agencies, the drug and device industry, research universities and institutes, the patient community, health plans, providers and others. Such thoughtful and forward-looking proposals are what made us so excited about the Initiative in the first place, and we applaud the Committee for developing and including this provision in the discussion draft. We look forward to the opportunity to discuss this provision in more detail with the Committee.

We hope this feedback proves informative to the Committee as you continue to progress with the Initiative. We also recognize that we have not commented on every provision, many of which we are also generally supportive of.

Once again, CHI thanks you and your staff for your thoughtful and visionary leadership in launching the Initiative. We are pleased and encouraged by the content of the discussion draft and look forward to serving as a partner in advancing these proposals along the legislative process.

Please let me know if CHI can be of any further or additional assistance.

Sincerely,

A black rectangular box redacting the signature of Todd E. Gillenwater.

Todd E. Gillenwater  
Senior Vice President, Public Policy



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February 20, 2015

Chairman Fred Upton  
House Energy and Commerce Committee  
2125 Rayburn HOB  
Washington, DC, 20515

Congresswoman Diana DeGette  
House Energy and Commerce Committee  
2322A, Rayburn HOB  
Washington, DC 20515

Re: Request for Comments on *21<sup>st</sup> Century Cures Act*

Dear Chairman Upton and Congresswoman DeGette:

On behalf of the Cancer Support Community (CSC), an international nonprofit organization that provides support, education and hope to over 1 million people affected by cancer each year, we appreciate the opportunity to respond to a request for comment on the *21<sup>st</sup> Century Cures Act*. We applaud your efforts to put patients first in this legislation and encourage you to actively engage the patient community as this important initiative continues to unfold. CSC respectfully submits the following comments for your consideration.

**Comprehensive Care in Clinical Trials:**

CSC strongly urges the Committee to improve upon the draft by ensuring that distress screening for patients enrolled in clinical trials, and supportive care for those patients who show signs of distress, becomes a routine part of the clinical trial process. You will find our suggested language below, which includes an important incentive for companies that sponsor clinical trials to incorporate distress screening and supportive care into their studies.

Research has shown that nearly 50 percent of patients with cancer experience psychological, social, or economic distress, and that this form of distress can have a significant negative effect on the patient's ability to complete a course of therapy. In a clinical trial context, a patient's personal distress level can have a profound effect on the patient's ability to participate in all protocol-mandated visits, tests, treatments, and follow-up appointments. Each time a patient is unable to adhere to the requirements of the study, or fails altogether to complete the study, the overall quality and statistical power of the study is weakened.

With proper screening and intervention, research shows that we can reduce distress levels by 25 percent. Moreover, it is likely that by identifying and addressing patient distress levels, we will improve each patient's prospect for retention in the trial and his or her adherence to the protocol. Given the fact that a mere 3% of eligible patients enroll in an oncology clinical trial, and that patients have significantly better health outcomes when screened and treated for distress, we believe distress screening and supportive care will lead to more efficient use of clinical trial resources and have a positive impact on patient outcomes. In order to meaningfully advance cures in the 21<sup>st</sup> Century, we must do a far better job of recruiting and retaining patients in clinical trials. A true focus on patient-centered needs and concerns and the application of evidence-based interventions would dramatically improve participation, outcomes and satisfaction. Therefore, we strongly urge the Committee to pass this language.

### **Structured Risk Benefit Assessment Framework:**

We would like to express our support for the Structured Risk-Benefit Assessment Framework provision in the bill. CSC supports the intent of this language which would help ensure that the patient experience is considered in any risk-benefit assessment. However, we believe there is opportunity to strengthen this section of the legislation by integrating patient-focused incentives, including psychosocial distress screening and follow up care into the assessment. The legislative language below provides a strong framework for how this patient focused care can be achieved.

Furthermore, CSC believes that the patient-centered themes outlined in the title should be a mandatory part of the assessment, management and risk-benefit review for all patients who participate in a clinical trial. This type of intervention would ensure that we are proactively assessing components of care for the whole patient that are often not a part of biomedical assessments, yet have considerable impact on the overall experience. CSC believes that the measurement and inclusion of distress-related data is essential in understanding the patient's comprehensive needs, and should be incorporated into the clinical trials protocol. Integrating this data will not only allow us to better understand the key elements of the patient experience but also improve patient adherence to the clinical trial requirements.

### **Patient Experience Data:**

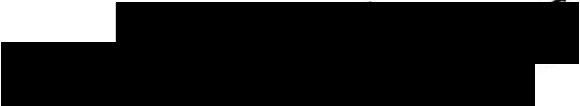
We appreciate the guidance drafted in the bill related to the Patient Experience Data. However, we urge you to include both the social and emotional aspects of the disease as a part of that guidance. The benefit of psychosocial support as a part of comprehensive care has been well known and documented. Most notably, the Institute of Medicine 2008 report *Cancer Care for the Whole Patient* specifically states, "Today, it is not possible to deliver good-quality cancer care without using existing approaches, tools, and resources to address patients' psychosocial health needs." Including the social and emotional aspects of the disease within the Patient Experience Data will ensure that patients are getting the highest quality of care.

### **Methodology Workshop and Patient Feedback:**

CSC supports the inclusion of language regarding the creation of workshops to seek feedback regarding methodological approaches. CSC fully believes there is an opportunity for patients to provide substantive feedback throughout this process. However, aligned with feedback provided to the [FDA on December 4, 2015](#), CSC is concerned that the feedback may not be a comprehensive perspective given the inability of many to attend in person due to physical, geographic or other limitations. CSC is also concerned that local/regional bias related to access and care may contribute to limited information. CSC encourages the agencies to make a larger commitment to securing feedback by working with patient groups, community organizations and other mechanisms that allow the collection of a more comprehensive view of the patient experience.

Again, thank you for your leadership and work on accelerating cures in the 21<sup>st</sup> Century. We look forward to working with you on this important effort.

Sincerely,



Kim Thiboldeaux  
Chief Executive Officer